

LAW OFFICES

KELLER AND HECKMAN

1001 G STREET, N.W.

SUITE 500 WEST

WASHINGTON, D.C. 20001

TELEPHONE (202) 434-4100

TELEX 49 95551 "KELMAN"

TELECOPIER (202) 434-4646

BOULEVARD LOUIS SCHMIDT 87

B-1040 BRUSSELS

TELEPHONE 32(2) 732 52 80

TELECOPIER 32(2) 732 53 92

JOSEPH E. KELLER (1907-1994)
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*NOT ADMITTED IN D.C.
 *RESIDENT BRUSSELS

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 CHARLES V. BREDER, Ph. D.
 ROBERT A. MATHEWS, Ph. D., D.A.B.T.
 JOHN P. MODDERMAN, Ph. D.
 HOLLY HUTMIRE FOLEY
 JUSTIN C. POWELL, Ph. D.
 JANETTE HOUK, Ph. D.
 LESTER BORODINSKY, Ph. D.
 THOMAS C. BROWN
 TELECOMMUNICATIONS
 ENGINEER
 CHARLES F. TURNER
 WRITER'S DIRECT DIAL NUMBER

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Re: TSCA 8(e) Filing

Dear Sir or Madam:

At the request of our client, Velsicol Chemical Corporation, we are delivering the following final toxicity study report in conformance with section 8(e) of Toxic Substances Control Act (TSCA) (15 U.S.C. § 2607(e)):

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

The test substance is subject to a 5(e) consent order for PMN P-90-549 (CASRN 131298-44-7).

In this study, which involved dosing rats at 30, 300, and 1000 mg/kg/day, maternal toxicity was exhibited at a dose level of 1000 mg/kg/day by a transient mean body weight loss during the first three days of dosing. Developmental toxicity was exhibited at this dose level by a slight decrease in fetal body weight and reduced incidence of cervical centrum number one ossified. No maternal toxicity or developmental toxicity was observed at the lower dose levels.

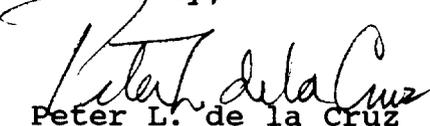
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If you have any questions concerning this submission, please contact me at 202-434-4141 or Mr. David J. Mason at Velsicol at 708-635-3422.

Sincerely,



Peter L. de la Cruz

Enclosure

cc: Ken Moss
OPPT/CCD/NCB

Phillip K. Cobb, Esq.
David J. Mason



FINAL REPORT

STUDY TITLE

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

DATA REQUIREMENT

40 CFR Part 798.4900

STUDY DIRECTOR

John F. Knapp, B.S.

STUDY INITIATED ON

August 4, 1994

STUDY COMPLETED ON

February 10, 1995

PERFORMING LABORATORY

WIL Research Laboratories, Inc.
1407 George Road
Ashland, OH 44805-9281

LABORATORY STUDY NUMBER

WIL-15218

SPONSOR

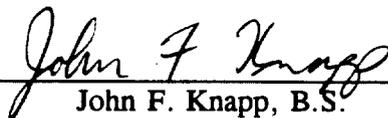
Velsicol Chemical Corporation
10400 W. Higgins Road; Suite 600
Rosemont, Illinois 60018-3713

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A Developmental Toxicity Study of Isodecyl Benzoate in Rats

STATEMENT OF GOOD LABORATORY PRACTICE COMPLIANCE

This study, designated WIL-15218, was conducted in compliance with the United States Environmental Protection Agency (EPA) Toxic Substances Control Act (TSCA) Good Laboratory Practice Regulations (40 CFR Part 792), August 17, 1989, and Health Effects Testing Guidelines for Developmental Toxicity Studies (40 CFR Part 798.4900), May 20, 1987, and the Standard Operating Procedures of WIL Research Laboratories, Inc. The study was conducted in accordance with the protocol and protocol amendments as approved by the sponsor.



John F. Knapp, B.S.
Study Director

2/10/95
Date



2/16/95

DAVID J. MASON, M.S.
Director, SHEA
Velsicol Chemical Corporation

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

TABLE OF CONTENTS

| | <u>Page</u> |
|--|-------------|
| I. Summary | 8 |
| II. Objective | 10 |
| III. Study Design | 11 |
| IV. Experimental Procedures | 12 |
| A. Introduction | 12 |
| B. Test and Control Materials | 12 |
| 1. Test Material Identification | 12 |
| 2. Vehicle Control Material Identification | 12 |
| 3. Preparation | 13 |
| 4. Administration | 13 |
| 5. Sampling and Analyses | 14 |
| C. Animal Receipt and Acclimation | 14 |
| D. Animal Housing | 14 |
| E. Diet, Drinking Water and Maintenance | 15 |
| F. Environmental Conditions | 15 |
| G. Assignment of Animals to Treatment Groups and Breeding Procedures | 15 |
| H. Maternal Observations During Gestation | 16 |
| 1. Clinical Observations and Survival | 16 |
| 2. Body Weights and Gravid Uterine Weights | 16 |
| 3. Food Consumption | 17 |
| I. Gestation Day 20 Laparohysterectomy | 17 |
| J. Fetal Morphological Examination | 18 |
| K. Statistical Analyses | 19 |
| L. Data Retention | 20 |
| V. Results | 21 |
| A. Clinical Observations and Survival | 21 |
| B. Body Weights and Gravid Uterine Weights | 21 |

| | <u>Page</u> |
|---|-------------|
| C. Food Consumption | 22 |
| D. Necropsy Data | 22 |
| E. Gestation Day 20 Laparohysterectomy Data | 22 |
| F. Fetal Morphological Data | 23 |
| 1. External Malformations and Variations | 23 |
| 2. Visceral Malformations and Variations | 23 |
| 3. Skeletal Malformations and Variations | 23 |
| 4. Summary of External, Visceral and Skeletal Examinations | 25 |
| VI. Discussion and Conclusions | 26 |
| VII. Key Study Personnel and Report Submission | 28 |
| VIII. Quality Assurance Unit Statement | 29 |
| IX. References | 30 |

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

INDEX OF TABLES

| | <u>Page</u> |
|---|-------------|
| 1. Summary of Maternal Survival and Pregnancy Status | 32 |
| 2. Summary of Clinical Findings: Total Occurrence/No. of Animals (Daily Examinations) | 33 |
| 3. Summary of Clinical Findings: Total Occurrence/No. of Animals (1-Hour Post-Dosing) | 35 |
| 4. Mean Body Weights (Grams) During Gestation | 36 |
| 5. Mean Body Weight Changes (Grams) During Gestation | 38 |
| 6. Mean Gravid Uterine Weights and Net Body Weight Changes (Grams) | 40 |
| 7. Mean Food Consumption During Gestation (Grams/Animal/Day) | 41 |
| 8. Mean Food Consumption During Gestation (Grams/Kg/Day) | 42 |
| 9. Summary of Mean Fetal Data at the Scheduled Necropsy | 43 |
| 10. Summary of Mean Fetal Data at the Scheduled Necropsy (% per Litter) | 44 |
| 11. Number of Fetuses and Litters with Malformations - Summary | 47 |
| 12. Percent of Fetuses and Litters with Malformations - Summary | 48 |
| 13. Mean Litter Proportions of Malformations - Summary | 49 |
| 14. Number of Fetuses and Litters with Variations - Summary | 53 |
| 15. Percent of Fetuses and Litters with Variations - Summary | 54 |
| 16. Mean Litter Proportions of Variations - Summary | 55 |

| | <u>Page</u> |
|---|-------------|
| 17. Individual Clinical Observations (Daily Examinations) | 60 |
| 18. Individual Clinical Observations (1-Hour Post-Dosing) | 74 |
| 19. Individual Body Weights (Grams) During Gestation | 75 |
| 20. Individual Body Weight Changes (Grams) During Gestation | 83 |
| 21. Individual Gravid Uterine Weights and Net Body Weight Changes (Grams) | 91 |
| 22. Individual Food Consumption During Gestation (Grams/Animal/Day) | 95 |
| 23. Individual Food Consumption During Gestation (Grams/Kg/Day) | 99 |
| 24. Individual Dam Gross Necropsy Examinations | 103 |
| 25. Individual Fetal Data at the Scheduled Necropsy | 107 |
| 26. Individual Fetal Data at the Scheduled Necropsy (% per Litter) | 111 |
| 27. Individual Fetal Weights (Grams) | 115 |
| 28. Individual Fetal External, Visceral and Skeletal Findings | 119 |

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

INDEX OF APPENDICES

| | <u>Page</u> |
|--|-------------|
| A. Analysis of Dosing Preparations (WIL Research Laboratories, Inc.) | 172 |
| B. WIL Historical Control Data (Sprague-Dawley CrI:CD®BR Rats) - Summary | 187 |
| C. WIL Historical Control Data (Sprague-Dawley CrI:CD®BR Rats) - Individual | 195 |
| D. Study Protocol | 274 |

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

I. SUMMARY

The potential maternal toxicity and developmental toxicity of Isodecyl Benzoate were evaluated. Isodecyl Benzoate in Mazola® corn oil was administered orally by gavage to three groups of 25 bred Sprague-Dawley Crl:CD®BR female rats once daily from gestation days 6 through 15. Dosage levels were 30, 300 and 1000 mg/kg/day administered at a dose volume of 5 ml/kg. A concurrent control group composed of 25 bred females received the vehicle, Mazola® corn oil, on a comparable regimen at 5 ml/kg. All rats were observed twice daily for appearance and behavior. Body weights and food consumption were recorded at appropriate intervals. A laparohysterectomy was performed on all animals on gestation day 20. The uteri and ovaries were examined and the numbers of fetuses, early and late resorptions, total implantations and corpora lutea were recorded. Mean gravid uterine weights and net body weight changes were calculated for each group. The fetuses were weighed, sexed and examined for external, soft tissue and skeletal malformations and developmental variations.

All maternal animals survived to the scheduled necropsy; no clinical signs related to compound administration were noted in the treated groups. A mean body weight loss occurred in the 1000 mg/kg/day group during gestation days 6-9. Food consumption was unaffected by treatment throughout the study period in all dose groups. No treatment-related internal findings were observed at necropsy. The only adverse effects of treatment on the developing fetus were a decrease in the mean fetal body weight and a reduction in the incidence of cervical centrum no. 1 ossified (both of which are indications of developmental retardation in the fetuses) in the 1000 mg/kg/day group. No other treatment-related malformations or developmental variations were observed at any dose level.

In conclusion, maternal toxicity was exhibited at a dose level of 1000 mg/kg/day by a transient mean body weight loss. Developmental toxicity was exhibited at a dose level of 1000 mg/kg/day by a slight decrease in mean fetal body weight and a reduction in the incidence of cervical centrum no. 1 ossified. Based on the results of this study,

WIL-15218
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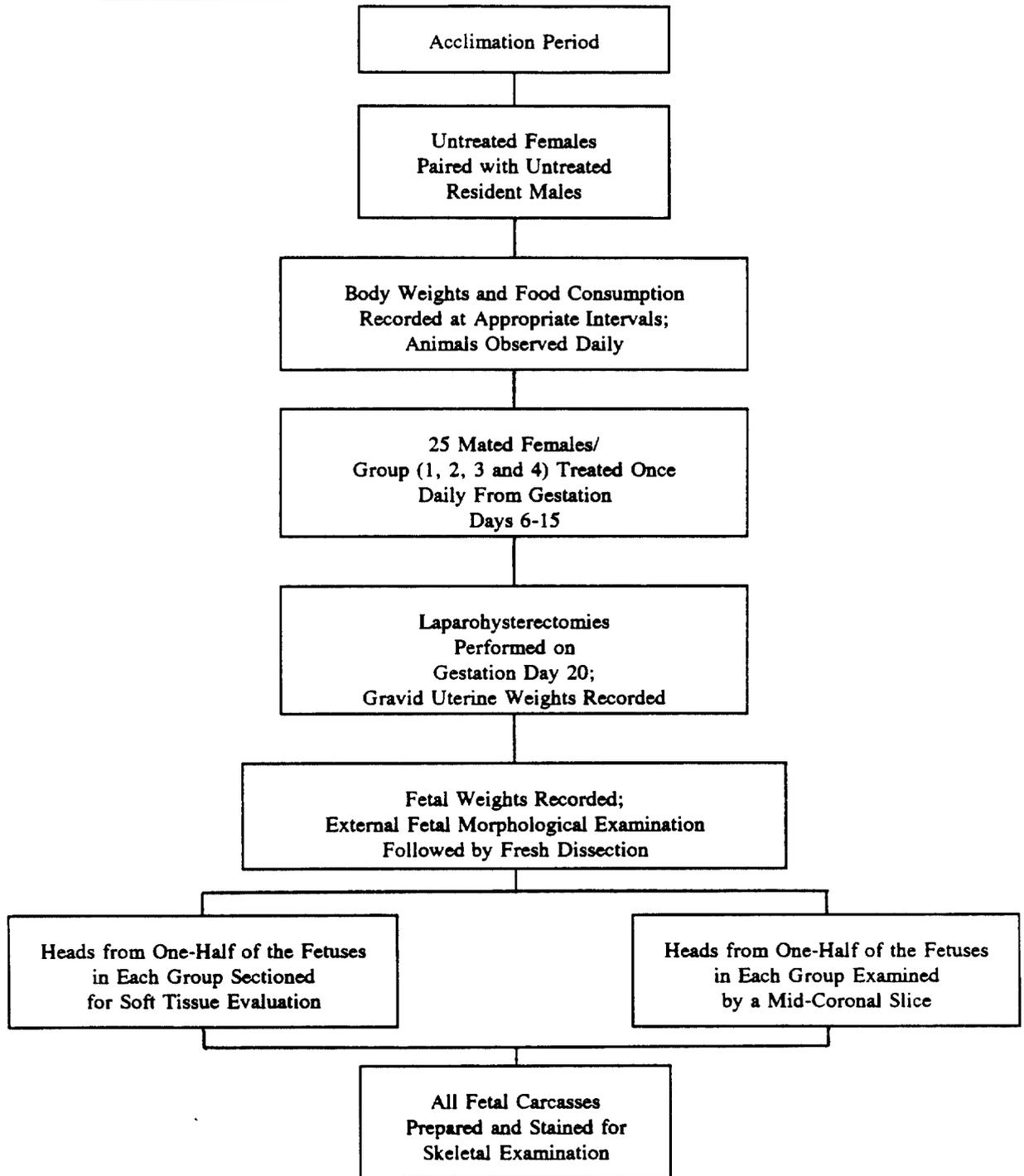
a dose level of 300 mg/kg/day was considered to be the NOAEL (no observable adverse effect level) for maternal toxicity and developmental toxicity.

II. OBJECTIVE

The objective of the study was to investigate the potential maternal and/or developmental toxicity of Isodecyl Benzoate in Sprague-Dawley CrI:CD®BR rats.

The selected route of administration was oral because this is the anticipated route of exposure for the general human population. The animal model was selected based on the availability of historical control data and the susceptibility of the species to known developmental toxicants.

III. STUDY DESIGN



IV. EXPERIMENTAL PROCEDURES

A. INTRODUCTION

The experimental phase of the study was initiated with the assignment of mated rats to treatment groups on August 23, 1994, and concluded with the last laparohysterectomy on September 16, 1994; the dosing period was from August 29, 1994, to September 11, 1994. Dose levels were selected based on the results of a dosage range-finding developmental toxicity study of Isodecyl Benzoate in rats (WIL-15217¹).

B. TEST AND CONTROL MATERIALS

1. TEST MATERIAL IDENTIFICATION

Isodecyl Benzoate was received from Velsicol Chemical Corporation, Chattanooga, Tennessee, on June 14, 1994, as follows:

| <u>Label Identification</u> | <u>Quantity Received</u> | <u>Description</u> |
|--|---|---------------------------|
| Isodecyl Benzoate Batch C5-8 5/15/94 | 2 Bottles Gross weight: 1) 1260.8 g ^a 2) 1254.5 g | Clear colorless liquid |

^a - Bottle used in WIL-15218

Stability and purity data were the responsibility of the sponsor. The bulk material was approximately 98% mixed C_{9,11} isomers. However, for purposes of dose calculations, the test material was considered to be 100% Isodecyl Benzoate. The test material was considered stable when stored at room temperature. A reserve one gram sample of the bulk test material was taken on June 15, 1994, and stored in the Archives at WIL Research Laboratories, Inc.

2. VEHICLE CONTROL MATERIAL IDENTIFICATION

The vehicle control material utilized in preparation of the test mixtures was Mazola[®] corn oil, manufactured by Best Foods, CPC International, Inc., General Offices, Englewood Cliffs, New Jersey:

| <u>Label Identification</u> | <u>No. of Containers Received</u> | <u>Physical Description</u> | <u>Dates</u> |
|-----------------------------|-----------------------------------|-----------------------------|--|
| Mazola 100% Corn Oil | 6-one gallon jugs | Yellow viscous liquid | Received: 6/15/94 Expiration: 3/15/95 |

3. PREPARATION

An appropriate amount of the vehicle, Mazola® corn oil, was dispensed into a properly-labeled storage container for administration to the control group. An appropriate amount of the test material, Isodecyl Benzoate, was weighed for each group into tared, precalibrated storage containers. A sufficient amount of the vehicle, Mazola® corn oil, was added to bring the volume to the calibration mark. The preparations were placed on the Polytron® PT 6000 laboratory mixer for approximately 5 minutes. A stir bar was added, and the dosing suspensions were stirred on a magnetic stir plate throughout the sampling and dosing procedures. Preparations for all dose groups were formulated three times (August 26, September 2, and September 9, 1994) and were stored refrigerated.

4. ADMINISTRATION

The dosing preparations were administered orally by gavage, via a 16-gauge stainless steel gavage cannula (Popper and Sons, Inc., New Hyde Park, New York 11040), as a single daily dose from gestation days 6 through 15. A dosage volume of 5 ml/kg was used for all dosage levels. The control animals received Mazola® corn oil on a comparable regimen of 5 ml/kg. Individual dosages were based on the most recently recorded body weight to provide the correct mg/kg/day dose. The following diagram presents the study group assignment:

| <u>Group Number</u> | <u>Test Substance</u> | <u>Dosage Level (mg/kg/day)</u> | <u>Dosage Concentration (mg/ml)</u> | <u>Dosage Volume (ml/kg)</u> | <u>Number of Females</u> |
|---------------------|-----------------------|---------------------------------|-------------------------------------|------------------------------|--------------------------|
| 1 | Mazola® Corn Oil | 0 | 0 | 5 | 25 |
| 2 | Isodecyl Benzoate | 30 | 6 | 5 | 25 |
| 3 | Isodecyl Benzoate | 300 | 60 | 5 | 25 |
| 4 | Isodecyl Benzoate | 1000 | 200 | 5 | 25 |

5. SAMPLING AND ANALYSES

Aliquots were obtained from each dose level following each dose preparation and were analyzed for concentration prior to administration to the animals. The results of the analyses are presented in Appendix A. The preparations used to dose the animals contained the amounts of test material specified in the protocol.

The homogeneity and stability (8-day under refrigeration) of the test material in the vehicle were previously established in a dose range-finding study (WIL-15217)¹.

C. ANIMAL RECEIPT AND ACCLIMATION

One hundred twenty-five sexually mature, virgin female Sprague-Dawley Crl:CD®BR rats were received in good health from Charles River Breeding Laboratories, Inc., Portage, Michigan, on August 11, 1994. The animals were approximately 75 days old upon receipt. Upon receipt, each animal was observed by a qualified technician. The animals were weighed the day following receipt. All animals were uniquely identified by a Monel® metal eartag displaying the animal number and housed for 12 days for acclimation purposes. During this time, the animals were observed twice daily for mortality and moribundity.

D. ANIMAL HOUSING

Upon arrival and until pairing, all animals were individually housed in clean, wire-mesh cages suspended above cage-board. The animals were paired for mating in the home cage of the male. Following positive identification of mating, the females were returned to an individual suspended wire-mesh cage. Animals were maintained in accordance with the National Institutes of Health "Guide for

the Care and Use of Laboratory Animals"². The animal facilities at WIL Research Laboratories, Inc., are accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

E. DIET, DRINKING WATER AND MAINTENANCE

The basal diet used in this study was Purina[®] Certified Rodent Chow[®] #5002. This diet is a certified feed with appropriate analyses performed by the manufacturer and provided to WIL Research Laboratories, Inc. Municipal water supplying the facility is sampled for contaminants according to Standard Operating Procedures. The results of these analyses are maintained at WIL Research Laboratories, Inc. No contaminants were present in animal feed or water at levels expected to interfere with the objectives of this study. Drinking water delivered by an automatic watering system and the basal diet were provided *ad libitum* throughout the acclimation period and during the study.

F. ENVIRONMENTAL CONDITIONS

All animals were housed throughout the acclimation period and during the study in an environmentally-controlled room. Controls were set to maintain temperature at 72° ± 3°F and a relative humidity of 40-80%. Room temperature and relative humidity were recorded daily. The temperature ranged from 65° to 71°F, and the relative humidity ranged from 58% to 82% during the study period. The occasional deviations from the set temperature and humidity levels did not apparently affect the outcome of the study. Light timers were calibrated to provide a 12-hour light/12-hour dark photoperiod. Air handling units were set to provide approximately 10 fresh air changes per hour.

G. ASSIGNMENT OF ANIMALS TO TREATMENT GROUPS AND BREEDING PROCEDURES

At the conclusion of the acclimation period, all available females were weighed and examined in detail for physical abnormalities. At the discretion of the study director, animals judged to be in good health and meeting acceptable body weight requirements (a minimum of 220 g) were placed in a suspended wire-mesh cage with a resident male from the same strain and source for breeding. Resident males were untreated, sexually mature rats utilized exclusively for

breeding. These males were maintained under similar laboratory conditions as the females. The animals were paired on a 1:1 basis. A breeding record containing the male and female identification numbers and the dates of cohabitation was prepared. The selected females were approximately 12 weeks old when paired for breeding.

Positive evidence of mating was confirmed by the presence of a copulatory plug or the presence of sperm in a vaginal smear. Each mating pair was examined daily. The day on which evidence of mating was identified was termed day 0 of gestation and the animals were separated.

The experimental design for WIL-15218 consisted of three Isodecyl Benzoate treated groups and one control group. The bred females were consecutively assigned in a block design to groups containing 25 rats each by the following randomization procedure. The first mated female and the appropriate gestation day 0 designation were recorded, and the female was assigned to group 1, the second mated female was assigned to group 2, and the third to group 3, etc. This process was continued daily until 25 females were placed into each group. Body weight values ranged from 220 g to 279 g on day 0 of gestation.

H. MATERNAL OBSERVATIONS DURING GESTATION

1. CLINICAL OBSERVATIONS AND SURVIVAL

All rats were observed twice daily for moribundity and mortality. Detailed clinical observations were recorded individually from days 0 through 20 of gestation. Observations were recorded before dosing during the dosing period. Animals were also observed for signs of toxicity approximately one hour following treatment throughout the dosing period. All significant findings were recorded at the post-dosing observation periods.

2. BODY WEIGHTS AND GRAVID UTERINE WEIGHTS

Individual maternal body weights were recorded on gestation days 0, 6-16 and 20. A group mean body weight was calculated for each of these days. Mean body weight changes were calculated for each corresponding interval and also for days 6-9, 9-12, 12-16, 6-16 and 0-20.

Gravid uterine weight was collected and net body weight (the day 20 body weight minus the weight of the uterus and contents) and net body weight change (the day 0-20 body weight change minus the weight of the uterus and contents) were calculated and presented for each gravid female at the scheduled laparohysterectomy.

3. FOOD CONSUMPTION

Individual food consumption was recorded on gestation days 0, 6, 9, 12, 16 and 20. Food intake was reported as g/animal/day and g/kg/day for each corresponding body weight change interval.

I. GESTATION DAY 20 LAPAROHYSTERECTOMY

All maternal animals were euthanized by carbon dioxide inhalation on gestation day 20. The thoracic, abdominal and pelvic cavities were opened by a ventral mid-line incision, and the contents were examined. In all instances, the *post mortem* findings were correlated with the *ante mortem* comments and any abnormalities were recorded. The uterus and ovaries were excised, and the number of corpora lutea on each ovary was recorded. The trimmed uterus was weighed and opened, and the number and location of all fetuses, early and late resorptions and the total number of implantation sites were recorded. The individual uterine distribution of implantation sites was documented using the following procedure. All implantation sites, including resorptions, were numbered in consecutive order beginning with the left distal to the left proximal uterine horn, noting the position of the cervix, and continuing from the right proximal to the right distal uterine horn. Maternal tissues were preserved in 10% neutral buffered formalin for possible future histopathological examination only as indicated by the gross findings. The carcass of each dam was then discarded.

Uteri with no macroscopic evidence of nidation were excised, opened and subsequently placed in 10% ammonium sulfide solution for detection of early implantation loss as described by Salewski³.

Intrauterine data were summarized using two methods of calculation. An example of each method of calculation follows:

1. Group Mean Litter Basis:

$$\text{Postimplantation Loss/Litter} = \frac{\text{No. Dead Fetuses, Resorptions (Early/Late)/Group}}{\text{No. Gravid Females/Group}}$$

2. Proportional Litter Basis:

$$\text{Summation per Group (\%)} = \frac{\text{Postimplantation Loss/Litter (\%)}^4}{\text{No. of Litters/Group}}$$

$$a = \frac{\text{No. Dead Fetuses, Resorptions (Early/Late)/Litter}}{\text{No. Implantation Sites/Litter}} \times 100$$

J. FETAL MORPHOLOGICAL EXAMINATION

Each fetus was sexed, weighed and tagged for identification. Fetal tags contained the WIL study number, the female number and the fetus number. A detailed external examination of each fetus was conducted to include, but was not limited to, the eyes, palate and external orifices, and each finding was recorded. Crown-rump measurements were recorded for late resorptions, if present, and the tissues were discarded. Each fetus was examined viscerally by a modification of the Stuckhardt and Poppe⁴ fresh dissection technique to include the heart and major vessels. The sex of each fetus was verified by an internal examination. The sex of one fetus each in the litters of dam nos. 29634, 29595 and 29607 in the control, 30 and 300 mg/kg/day groups, respectively, was changed from female to male (nos. 29634 and 29607) or from male to female (no. 29595). However, because the fetus numbers were not recorded, the edits could not be made in the study data. Fetal kidneys were examined and graded for renal papillae development by a method described by Woo and Hoar⁵.

Heads from approximately one-half of the fetuses in each litter were placed in Bouin's fixative for subsequent soft-tissue examination by the Wilson⁶ sectioning technique. The heads from the remaining one-half of the fetuses were examined by a mid-coronal slice. All carcasses were eviscerated and fixed in 100% ethyl alcohol. Following fixation in alcohol, each fetus was macerated in potassium

hydroxide and stained with Alizarin Red S by a method similar to that described in Dawson⁷. The skeletal examination was conducted utilizing low power magnification provided by a stereomicroscope. External, visceral and skeletal findings were recorded as developmental variations or malformations.

The fetal developmental findings were summarized by: 1) presenting the incidence of a given finding both as a percentage of the no. of fetuses and the no. of litters available for examination in the group; and 2) considering the litter as the basic unit for comparison and calculating the no. of affected fetuses in a litter on a proportional basis as follows:

$$\text{Summation per Group (\%)} = \frac{\text{Viable Fetuses Affected/Litter (\%)}^a}{\text{No. of Litters/Group}}$$

$$a = \frac{\text{No. Viable Fetuses Affected/Litter}}{\text{No. Viable Fetuses/Litter}} \times 100$$

K. STATISTICAL ANALYSES

All analyses were conducted using two-tailed tests for a minimum significance level of 5% comparing each treated group to the vehicle control group. Each mean was presented with the standard deviation (S.D.) and the number of animals (N) used to calculate the mean. The following statistical tests were performed by a Digital[®] MicroVAX[®] 3400 computer (with appropriate programming) in this laboratory and are referenced on the report tables:

| <u>STATISTICAL TEST</u> | <u>PARAMETER</u> |
|--|--|
| - Chi-square test ^a with Yates' correction factor | Fetal Sex Ratios |
| - Fisher's Exact test ^a | Malformations and Variations |
| - Mann-Whitney U-test ^a | Early and Late Resorptions, Dead Fetuses, Postimplantation Losses, Mean Litter Proportions of Malformations and Variations |

STATISTICAL TEST

PARAMETER

- One-way ANOVA with
Dunnett's test⁸

Corpora Lutea, Total Implantations, Viable Fetuses, Fetal Body Weights, Maternal Body Weights and Weight Changes, Maternal Net Body Weight Changes, Gravid Uterine Weights, Maternal Food Consumption

- Kruskal-Wallis test⁸

Litter Proportions of Intrauterine Data (Considering the Litter, Rather than the Fetus, as the Experimental Unit)

L. DATA RETENTION

The sponsor will have title to all documentation records, raw data, specimens or other work product generated during the performance of the study. All work product including raw paper data and specimens will be retained in the Archives at WIL Research Laboratories, Inc., as specified in the protocol.

Raw data in magnetic form, a retention sample of the test material and the original final report will be retained in the Archives at WIL Research Laboratories, Inc., in compliance with regulatory requirements.

V. RESULTS

A. CLINICAL OBSERVATIONS AND SURVIVAL

Summary Data: Tables 1, 2, 3

Individual Data: Tables 17, 18

All animals survived to the scheduled necropsy on gestation day 20. No clinical signs related to compound administration were noted at any dose level during the daily observations or the observations made one hour following dosing. Observations in the 30, 300 and/or 1000 mg/kg/day groups that were unrelated to treatment included hair loss and scabbing on various body surfaces, wet brown staining in the anogenital and ventral abdominal areas, dried yellow staining in the urogenital area, dried red material on the ears, soft stool and tan feces. These findings occurred infrequently and/or at a similar frequency in the control group. Clinical observations noted during the examinations made one hour following dosing were limited to wet clear staining around the mouth in one animal (no. 29626) in the 1000 mg/kg/day group on gestation day 12.

B. BODY WEIGHTS AND GRAVID UTERINE WEIGHTS

Summary Data: Tables 4, 5, 6

Individual Data: Tables 19, 20, 21

A statistically significant ($p < 0.01$) group mean body weight loss occurred in the 1000 mg/kg/day group during gestation days 6-9. This decrease was due primarily to a statistically significant ($p < 0.01$) mean body weight loss during gestation days 6-7. Throughout the remainder of the study (gestation days 6-16, 9-12, 12-16 and 16-20), no differences were observed in mean body weight gains between the control and 1000 mg/kg/day groups. No remarkable differences were observed in the mean body weight gains in the 30 or 300 mg/kg/day groups relative to the control group throughout the study. Mean body weights, gravid uterine weights, net body weights and net body weight gains were not adversely affected by compound administration at any dose level.

C. FOOD CONSUMPTION

Summary Data: Tables 7, 8

Individual Data: Tables 22, 23

Food consumption, evaluated as g/animal/day and g/kg/day, was not affected by compound administration in the 30, 300 or 1000 mg/kg/day groups throughout the study. All treated group values were comparable to the control group values.

D. NECROPSY DATA

Individual Data: Table 24

No treatment-related internal findings were observed at the scheduled necropsy. Reddened lungs were observed in one animal (no. 29647) in the control group, one animal (no. 29648) in the 300 mg/kg/day group and two animals (nos. 29654 and 29659) in the 1000 mg/kg/day group. Other findings included an accessory spleen in one animal (no. 29602) in the control group, fused placentas in one animal (no. 29607) in the 300 mg/kg/day group and a dilated renal pelvis in one animal (no. 29618) in the 1000 mg/kg/day group. All other animals were internally normal.

E. GESTATION DAY 20 LAPAROHYSTERECTOMY DATA

Summary Data: Tables 9, 10

Individual Data: Tables 25, 26, 27

Historical Control Data: Appendices B, C

The mean fetal body weight in the 1000 mg/kg/day group (3.3 g) was decreased relative to the control group value (3.6 g). This difference was statistically significant ($p < 0.01$). The 1000 mg/kg/day group value was within the range of the WIL historical control data (3.3-3.8 g). However, only 5 of 108 individual data sets (5%) in the historical control had mean fetal body weights of 3.3 grams. Therefore, this effect was considered to be treatment-related. The mean fetal body weights in the 30 and 300 mg/kg/day groups were not significantly different from the control group value. No other treatment-related effects were observed on intrauterine growth and survival. Postimplantation loss, fetal sex ratios, the number of viable fetuses and the numbers of implantation sites

and corpora lutea were not affected by compound administration in any of the treatment groups. The mean number of corpora lutea in the 300 mg/kg/day group (17.6) was increased relative to the control group value (15.6); this increase was statistically significant ($p < 0.05$). However, the number of corpora lutea is inherently determined, and no relationship to treatment was evident.

F. FETAL MORPHOLOGICAL DATA

Summary Data: Tables 11, 12, 13, 14, 15, 16

Individual Data: Table 28

Historical Control Data: Appendices B, C

The numbers of fetuses (litters) available for fetal morphological examination were 301(24), 327(22), 338(24) and 304(22) in the control, 30, 300 and 1000 mg/kg/day groups, respectively. The numbers of fetuses (litters) with malformations were 1(1), 2(2), 0(0) and 1(1) in these same dose groups, respectively.

1. EXTERNAL MALFORMATIONS AND VARIATIONS

Two fetuses in the 30 mg/kg/day group had external malformations. Fetus no. 29666-02 had anophthalmia and exencephaly with ablepharia, and fetus no. 29673-15 had a filamentous tail.

No other external developmental malformations or variations were observed in fetuses at any dose level.

2. VISCERAL MALFORMATIONS AND VARIATIONS

Visceral malformations were observed in one fetus each in the control and 1000 mg/kg/day groups. Fetus no. 29599-14 in the control group had a heart and great vessel anomaly. Fetus no. 29641-04 in the 1000 mg/kg/day group had situs inversus.

Visceral variations were limited to distension of one or both ureters in fetus nos. 29617-03, 29629-14 and 29671-09 in the 30, 300 and 1000 mg/kg/day groups, respectively.

3. SKELETAL MALFORMATIONS AND VARIATIONS

The only skeletal malformation observed was a vertebral anomaly in one

fetus (no. 29666-02) in the 30 mg/kg/day group; this malformation consisted of the absence of two cervical arches and the fusion of a thoracic arch and a cervical arch.

Skeletal variations were observed in all dose groups, including the control group. Fourteenth rudimentary ribs were observed at an increased frequency in all of the treated groups relative to the control group (in 0 and 6 litters in the control and 1000 mg/kg/day groups, respectively). The increases in the fetal incidence of this variation appear to be dose-dependent. The litter incidence in the 300 and 1000 mg/kg/day groups was statistically significant ($p < 0.05$). The percentage of litters with 14th rudimentary ribs in the 300 and 1000 mg/kg/day groups was 25.0 and 27.3%, respectively, as compared with 0.0% for the control group. It should be noted that the control value for this developmental variation was atypically below historical control values. In the WIL historical control data, the modal distribution for the incidence of this variation in 108 definitive data sets was as follows:

Modal Distribution of Control Litters with 14th Rudimentary Ribs

| % of Litters Affected per Group | 0 | 1-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-100 |
|------------------------------------|---|------|-------|-------|-------|-------|-------|--------|
| No. of Definitive Data Sets | 6 | 18 | 27 | 16 | 19 | 10 | 5 | 7 |

This modal distribution demonstrates that 1) a degree of variability exists in the expression of this skeletal variant and 2) that the incidence in the intermediate and high dose levels in the present study has been observed frequently in previous historical control data sets. Therefore, the occurrences in the treated groups (25.0% and 27.3% of litters in the 300 and 1000 mg/kg/day groups, respectively) were not considered to be biologically significant.

Skeletal variations occurring in all dose groups, including the control group, consisted of cervical centrum no. 1 ossified, 7th cervical ribs, sternbrae nos. 5 and/or 6 unossified, bent ribs and reduced ossification of the 13th ribs. Ossification of cervical centrum no. 1 was slightly reduced in the

1000 mg/kg/day group relative to the control group. This was a further indication of the developmental delay in these fetuses (also observed in the reduction in fetal body weight). The incidence of reduced ossification of the 13th ribs was significantly ($p < 0.05$) reduced in the 1000 mg/kg/day group relative to the control group.

Other skeletal variations occurring in the treated groups, including sternbrae nos. 1, 2, 3 and/or 4 unossified, 14th full ribs, 25 presacral vertebrae, pubis unossified and sternbrae malaligned, occurred infrequently and/or at a similar frequency in the control group.

4. SUMMARY OF EXTERNAL, VISCERAL AND SKELETAL EXAMINATIONS

The external and visceral malformations which occurred in the control, 30 and 1000 mg/kg/day groups were apparently spontaneous in origin (1, 2 and 1 fetuses, respectively, were affected). Developmental variations occurred in all dose groups. The incidence of cervical centrum no. 1 ossified was decreased in the 1000 mg/kg/day group relative to the control group; this was an indication of the developmental retardation of these fetuses. An increased incidence of fourteenth rudimentary ribs was observed in all of the treated groups relative to the control group. The frequency was within the range of the WIL historical control data, and the variation was considered to be spontaneous in origin. Other fetal developmental variations were observed at a limited frequency or at a frequency similar to that in the control group.

VI. DISCUSSION AND CONCLUSIONS

All animals survived to the scheduled necropsy; no treatment-related clinical signs were observed at the daily examinations or in the examinations made one hour after dosing.

A statistically significant mean body weight loss occurred in the 1000 mg/kg/day group during gestation days 6-9. The mean body weight changes in this group were similar to the control values throughout the remainder of the study (gestation days 6-16, 9-12, 12-16 and 16-20). No differences were observed in mean body weight changes in the 30 and 300 mg/kg/day groups relative to the control group at any time throughout the study. No adverse effects of compound administration on body weights, net body weights, net body weight changes or food consumption were observed at any dose level.

No treatment-related internal findings were observed at any dose level.

The mean fetal body weight in the 1000 mg/kg/day group was significantly ($p < 0.01$) reduced relative to the control group value (3.6 g and 3.3 g in the control and 1000 mg/kg/day groups, respectively). The 1000 mg/kg/day group value was within the range of the WIL historical control data (3.3-3.8 g). However, only 5 of 108 individual data sets (5%) in the historical control had mean fetal body weights of 3.3 grams. Therefore, this effect was considered to be treatment-related. Mean fetal body weights were unaffected by treatment in the 30 and 300 mg/kg/day groups. Other intrauterine parameters in the treated groups, including postimplantation loss, live litter size, fetal sex ratio and the mean numbers of corpora lutea and implantation sites, were unaffected by treatment at any dose level.

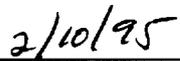
The numbers of fetuses (litters) available for fetal morphological examination were 301(24), 327(22), 338(24) and 304(22) in the control, 30, 300 and 1000 mg/kg/day groups, respectively. The numbers of fetuses (litters) with malformations were 1(1), 2(2), 0(0) and 1(1) in these same dose groups, respectively. These malformations were considered to be spontaneous in origin. The incidence of cervical centrum no. 1 ossified was reduced in the 1000 mg/kg/day group relative to the control group; this was an indication of the developmental retardation of these fetuses. Other

developmental variations were observed in all dose groups, but were infrequent, occurred at a similar frequency in the control group or were within the range of the WIL historical control data, and were not considered to be treatment-related.

In conclusion, maternal toxicity was exhibited at a dose level of 1000 mg/kg/day by a transient mean body weight loss during the first three days of dosing. Developmental toxicity was exhibited at a dose of 1000 mg/kg/day by a slight decrease in fetal body weight and a reduced incidence of cervical centrum no. 1 ossified. No maternal toxicity or developmental toxicity was observed at 30 and 300 mg/kg/day. Based on the results of this study, a dose level of 300 mg/kg/day was considered to be the no observable adverse effect level (NOAEL) for maternal toxicity and developmental toxicity.



John F. Knapp, B.S.
Study Director



Date

VII. KEY STUDY PERSONNEL AND REPORT SUBMISSION

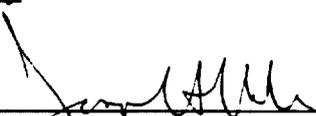
Study Supervisors:

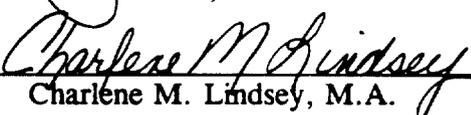
| | |
|------------------------|---|
| Melinda Bowen | Section Head I, Developmental and Reproductive Toxicology |
| Sally A. Keets, A.S. | Manager of In-Life Facilities |
| John F. Knapp, B.S. | Manager of Pharmacy |
| Kerin Clevidence, B.S. | Section Head II - Pathology and Developmental Toxicology Laboratory |

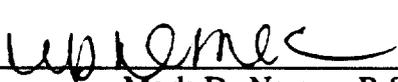
Report Preparation:

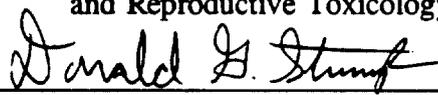
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|  _____ Ann S. Stump, Ph.D. Senior Report Writer | <u>2/10/95</u> Date |
|---|------------------------|

Reviewed By:

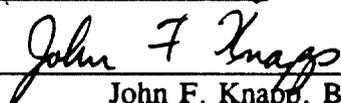
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|  _____ Joseph F. Holson, Ph.D. President, Director | <u>2/9/95</u> Date |
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|  _____ Charlene M. Lindsey, M.A. Manager of Technical Report Writing | <u>2/9/95</u> Date |
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|  _____ Mark D. Nemeck, B.S. Associate Director of Developmental and Reproductive Toxicology | <u>2/10/95</u> Date |
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|---|------------------------|
|  _____ Donald G. Stump, Ph.D. Associate Toxicologist, Developmental, Reproductive and Neurotoxicology | <u>2/10/95</u> Date |
|---|------------------------|

Approved and Submitted by:

| | |
|---|------------------------|
|  _____ John F. Knapp, B.S. Manager of Developmental, Reproductive and Neurotoxicology | <u>2/10/95</u> Date |
|---|------------------------|

VIII. QUALITY ASSURANCE UNIT STATEMENT

| <u>Date(s) of Inspection(s)</u> | <u>Phase Inspected</u> | <u>Date(s) Findings Reported to Study Director</u> | <u>Date(s) Findings Reported to Management</u> |
|---------------------------------|--|--|--|
| 8/22, 23/94 | Cohabitation and Confirmation of Breeding | 8/23/94 | 9/29/94 |
| 8/25/94 | Test Material Preparation and Administration | 8/26/94 | 9/29/94 |
| 8/25/94 | Animal Care and Equipment | 8/26/94 | 9/29/94 |
| 9/12/94 | Laparohysterectomy and Viscerals | 9/12/94 | 10/31/94 |
| 12/27/94, 1/4-6, 9-12/95 | Study Records (I-1, N-1) | 1/12/95 | 2/95 |
| 1/9, 11, 12/95 | Study Records (A-1, A-2) | 1/12/95 | 2/95 |
| 1/7-12, 15, 16/95 | Draft Report | 1/16/95 | 2/95 |

This study was conducted and inspected in accordance with the current EPA TSCA Good Laboratory Practice Regulations and Health Effects Testing Guidelines for Developmental Toxicity Studies, the Standard Operating Procedures of WIL Research Laboratories, Inc. and the sponsor's protocol and protocol amendment(s). Quality Assurance findings, derived from the inspections during the conduct of the study and from the inspections of the raw data and final report, are documented and have been reported to the study director. A status report is submitted to management monthly.

The raw data, the retention sample(s), if applicable, and the final report will be stored in the Archives at WIL Research Laboratories, Inc., or another location specified by the Sponsor.

Deborah L Little
Deborah L. Little
Manager of Quality Assurance

2/10/95
Date

IX. REFERENCES

1. WIL-15217, A dose range-finding developmental toxicity study of Isodecyl Benzoate in rats. WIL Research Laboratories, Inc., Ashland, Ohio.
2. NIH (1985) Guide for the Care and Use of Laboratory Animals. United States Department of Health and Human Services, Public Health Service, National Institutes of Health, NIH Publication No. 86-23, 83 pages.
3. Salewski (Köln), V.E. (1964) Farbemethode zum makroskopischen Nachweis von Implantationstellen am Uterus der Ratte. Naunyn - Schm. Archiv. für Exper. Pathologie und Pharm. 247:367.
4. Stuckhardt, J.L. and Poppe, S.M. (1984) Fresh visceral examination of rat and rabbit fetuses used in teratogenicity testing. Teratogenesis, Carcinogenesis and Mutagenesis 4:181-188.
5. Woo, D.C. and Hoar, R.M. (1972) Apparent hydronephrosis as a normal aspect of renal development in late gestation of rats: The Effect of Methyl Salicylate. Teratology 6:191-196.
6. Wilson, J.G. (1965) Embryological consideration in teratology. In: Teratology: Principles and Techniques. (Wilson, J.G. and Warkany, J., eds.) The University of Chicago Press, Chicago, Illinois, pp. 251-277.
7. Dawson, A.B. (1926) A note on the staining of the skeleton of cleared specimens with Alizarin Red S. Stain Technol. 1:123-124.
8. BMDP (1979) Biomedical Computer Programs. (Dixon, W.J. and Brown, M.B., eds.) University of California Press, Berkeley, CA, pp. 612, 780, 781.

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

TABLES 1 - 28

PROJECT NO.: WIL-15218
 SPONSOR: VELSCOIL

TABLE 1
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SUMMARY OF MATERNAL SURVIVAL AND PREGNANCY STATUS

| DOSE GROUP : | 1 | | 2 | | 3 | | 4 | |
|--|-----|-------|-----|-------|-----|-------|-----|-------|
| | NO. | % | NO. | % | NO. | % | NO. | % |
| FEMALES ON STUDY | 25 | | 25 | | 25 | | 25 | |
| FEMALES THAT ABORTED OR DELIVERED | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| FEMALES THAT DIED | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| FEMALES THAT ABORTED NONGRAVID | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| GRAVID | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| FEMALES THAT WERE EUTHANIZED NONGRAVID | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| GRAVID | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| FEMALES EXAMINED AT SCHEDULED NECROPSY NONGRAVID | 25 | 100.0 | 25 | 100.0 | 25 | 100.0 | 25 | 100.0 |
| GRAVID | 1 | 4.0 | 3 | 12.0 | 1 | 4.0 | 3 | 12.0 |
| WITH RESORPTIONS ONLY | 24 | 96.0 | 22 | 88.0 | 24 | 96.0 | 22 | 88.0 |
| WITH VIABLE FETUSES | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| | 24 | 100.0 | 22 | 100.0 | 24 | 100.0 | 22 | 100.0 |
| TOTAL FEMALES GRAVID | 24 | 96.0 | 22 | 88.0 | 24 | 96.0 | 22 | 88.0 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 2

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

| TABLE RANGE: | | 08-23-94 TO 09-16-94 | |
|--|---------|----------------------|---------|
| GROUP: | 1 | 2 | 3 |
| NORMAL | | | |
| -NO SIGNIFICANT CLINICAL OBSERVATIONS | 392/ 24 | 464/ 25 | 438/ 25 |
| DISPOSITION | | | |
| -SENT TO NECROPSY FOR SCHEDULED LAPAROHYSTRECTOMY; GESTATION DAY 20 | 25/ 25 | 25/ 25 | 25/ 25 |
| BODY/INTEGUMENT | | | |
| -HAIR LOSS RIGHT FORELIMB | 82/ 11 | 35/ 7 | 47/ 9 |
| -HAIR LOSS LEFT FORELIMB | 88/ 9 | 32/ 5 | 40/ 8 |
| -SCABBING RIGHT FORELIMB | 4/ 2 | 0/ 0 | 1/ 1 |
| -SCABBING LEFT FORELIMB | 4/ 2 | 0/ 0 | 3/ 2 |
| -WET BROWN STAINING ANOGENITAL AREA | 0/ 0 | 1/ 1 | 1/ 1 |
| -HAIR LOSS VENTRAL THORACIC AREA | 1/ 1 | 0/ 0 | 16/ 2 |
| -HAIR LOSS VENTRAL ABDOMINAL AREA | 10/ 1 | 5/ 1 | 24/ 3 |
| -HAIR LOSS LEFT LATERAL THORACIC AREA | 12/ 1 | 0/ 0 | 0/ 0 |
| -HAIR LOSS LEFT LATERAL ABDOMINAL AREA | 20/ 2 | 3/ 1 | 2/ 1 |
| -HAIR LOSS RIGHT LATERAL ABDOMINAL AREA | 17/ 2 | 12/ 2 | 4/ 2 |
| -HAIR LOSS RIGHT HINDLIMB | 18/ 2 | 6/ 1 | 21/ 2 |
| -HAIR LOSS LEFT HINDLIMB | 14/ 2 | 0/ 0 | 12/ 1 |
| -DRIED YELLOW STAINING UROGENITAL AREA | 0/ 0 | 0/ 0 | 0/ 0 |
| -HAIR LOSS RIGHT LATERAL THORACIC AREA | 8/ 1 | 1/ 1 | 3/ 1 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

100/ 8
84/ 7
8/ 3
2/ 1
4/ 2
1/ 1
8/ 1
0/ 0
6/ 1
0/ 0
4/ 1
1/ 1
0/ 0

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 2
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

| TABLE RANGE: | | 08-23-94 TO 09-16-94 | | | |
|--|--|----------------------|-------|-------|------|
| GROUP: | | 1 | 2 | 3 | 4 |
| BODY/INTEGUMENT | | | | | |
| -MET BROWN STAINING VENTRAL ABDOMINAL AREA | | 0/ 0 | 0/ 0 | 0/ 0 | 2/ 1 |
| -HAIR LOSS DORSAL ABDOMINAL AREA | | 4/ 1 | 2/ 1 | 0/ 0 | 0/ 0 |
| EYES/EARS/NOSE | | | | | |
| -DRIED RED MATERIAL LEFT MARGINAL EAR | | 15/ 2 | 13/ 3 | 20/ 4 | 2/ 1 |
| -DRIED RED MATERIAL RIGHT MARGINAL EAR | | 0/ 0 | 2/ 1 | 3/ 1 | 0/ 0 |
| EXCRETA | | | | | |
| -SOFT STOOL | | 1/ 1 | 1/ 1 | 0/ 0 | 0/ 0 |
| -TAN FECES | | 3/ 2 | 4/ 3 | 0/ 0 | 2/ 2 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

PROJECT NO.: WIL-15218
SPONSOR: VELSICOL

TABLE 3 (1-HOUR POST-DOSING)
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 08-29-94 TO 09-11-94
GROUP: 1 2 3 4

ORAL/DENTAL
-MET CLEAR STAINING AROUND MOUTH

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY 0/0 0/0 0/0 1/1

TABLE 4
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN BODY WEIGHTS (GRAMS) DURING GESTATION

| DAY | GROUP : | GROUP : | | | |
|--------|---------|---------|---------|---------|---------|
| | | 1 | 2 | 3 | 4 |
| DAY 0 | MEAN | 249. | 253. | 256. | 251. |
| | S.D./N | 9.3/24 | 11.8/22 | 12.9/24 | 14.6/22 |
| DAY 6 | MEAN | 280. | 279. | 283. | 283. |
| | S.D./N | 14.2/24 | 14.2/22 | 12.3/24 | 15.2/22 |
| DAY 7 | MEAN | 278. | 280. | 282. | 276. |
| | S.D./N | 14.2/24 | 14.7/22 | 14.9/24 | 15.6/22 |
| DAY 8 | MEAN | 280. | 282. | 283. | 276. |
| | S.D./N | 14.3/24 | 14.2/22 | 14.4/24 | 19.5/22 |
| DAY 9 | MEAN | 284. | 286. | 288. | 281. |
| | S.D./N | 12.0/24 | 13.3/22 | 14.9/24 | 17.5/22 |
| DAY 10 | MEAN | 289. | 292. | 294. | 286. |
| | S.D./N | 11.8/24 | 12.9/22 | 15.6/24 | 15.1/22 |
| DAY 11 | MEAN | 293. | 298. | 300. | 293. |
| | S.D./N | 12.6/24 | 15.4/22 | 16.0/24 | 14.0/22 |
| DAY 12 | MEAN | 299. | 303. | 305. | 298. |
| | S.D./N | 13.2/24 | 15.5/22 | 18.3/24 | 14.9/22 |
| DAY 13 | MEAN | 303. | 309. | 311. | 305. |
| | S.D./N | 13.9/24 | 16.5/22 | 16.8/24 | 14.5/22 |
| DAY 14 | MEAN | 308. | 313. | 317. | 309. |
| | S.D./N | 14.2/24 | 17.7/22 | 14.8/24 | 16.6/22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN BODY WEIGHTS (GRAMS) DURING GESTATION

| GROUP : | | 1 | 2 | 3 | 4 |
|---------|--------|---------|---------|---------|---------|
| DAY 15 | MEAN | 316. | 320. | 326. | 316. |
| | S.D./N | 14.8/24 | 18.6/22 | 17.1/24 | 16.4/22 |
| DAY 16 | MEAN | 327. | 328. | 336. | 327. |
| | S.D./N | 17.0/24 | 20.6/22 | 18.8/24 | 17.8/22 |
| DAY 20 | MEAN | 381. | 391. | 396. | 386. |
| | S.D./N | 26.6/24 | 27.0/22 | 28.4/24 | 25.5/22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

| GROUP : | | 1 | 2 | 3 | 4 |
|---------|-------------------|----------------|---------------|----------------|-----------------|
| DAY 0- | 6 MEAN S.D./N | 30. 11.4/24 | 26. 9.1/22 | 28. 10.5/24 | 32. 8.4/22 |
| DAY 6- | 7 MEAN S.D./N | -2. 5.4/24 | 1. 5.7/22 | -1. 5.5/24 | -7.** 6.1/22 |
| DAY 7- | 8 MEAN S.D./N | 2. 5.2/24 | 2. 5.0/22 | 1. 3.9/24 | 0. 9.0/22 |
| DAY 8- | 9 MEAN S.D./N | 3. 5.7/24 | 4. 4.5/22 | 5. 3.6/24 | 5. 7.7/22 |
| DAY 9- | 10 MEAN S.D./N | 5. 5.8/24 | 7. 5.6/22 | 6. 4.2/24 | 5. 4.9/22 |
| DAY 10- | 11 MEAN S.D./N | 5. 3.7/24 | 5. 4.2/22 | 6. 5.7/24 | 7. 5.9/22 |
| DAY 11- | 12 MEAN S.D./N | 5. 4.5/24 | 5. 5.0/22 | 5. 7.0/24 | 6. 4.8/22 |
| DAY 12- | 13 MEAN S.D./N | 5. 3.6/24 | 6. 3.5/22 | 6. 4.7/24 | 6. 3.7/22 |
| DAY 13- | 14 MEAN S.D./N | 5. 4.5/24 | 5. 4.8/22 | 6. 5.4/24 | 4. 3.8/22 |
| DAY 14- | 15 MEAN S.D./N | 8. 5.3/24 | 7. 6.0/22 | 10. 4.1/24 | 8. 4.1/22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

GROUP : 1 2 3 4

| | | | | |
|---------------------------|-----------------|-----------------|-----------------|-----------------|
| DAY 15- 16 MEAN S.D./N | 10. 4.4/24 | 8. 6.5/22 | 10. 4.0/24 | 11. 4.1/22 |
| DAY 16- 20 MEAN S.D./N | 54. 13.2/24 | 63. 10.9/22 | 60. 14.6/24 | 59. 11.4/22 |
| DAY 6- 9 MEAN S.D./N | 4. 6.7/24 | 6. 5.7/22 | 5. 5.9/24 | -2.** 5.4/22 |
| DAY 9- 12 MEAN S.D./N | 15. 6.3/24 | 17. 6.8/22 | 17. 6.9/24 | 17. 8.1/22 |
| DAY 12- 16 MEAN S.D./N | 28. 8.3/24 | 26. 7.9/22 | 32. 9.3/24 | 29. 6.3/22 |
| DAY 6- 16 MEAN S.D./N | 47. 11.9/24 | 49. 11.7/22 | 53. 12.3/24 | 44. 11.5/22 |
| DAY 0- 20 MEAN S.D./N | 132. 23.2/24 | 138. 18.6/22 | 141. 25.6/24 | 135. 21.5/22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 ** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING A TWO-TAILED DUNNETT'S TEST
 MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

PROJECT NO.: WIL-15218
 SPONSOR: VELSTOOL

TABLE 6
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN GRAVID UTERINE WEIGHTS AND NET BODY WEIGHT CHANGES (GRAMS)

| | GROUP: | | |
|---------------------|----------------------|----------------------|----------------------|
| | 1 | 2 | 3 |
| INITIAL BODY WT. | 249. 9.3 24 | 253. 11.8 22 | 256. 12.9 24 |
| TERMINAL BODY WT. | 381. 26.6 24 | 391. 27.0 22 | 396. 28.4 24 |
| GRAVID UTERINE WT. | 69.2 21.34 24 | 79.9 13.90 22 | 76.5 21.31 24 |
| NET BODY WT. | 312.0 14.91 24 | 311.2 16.92 22 | 319.9 16.51 24 |
| NET BODY WT. CHANGE | 62.5 11.40 24 | 58.2 11.17 22 | 64.1 15.70 24 |
| | | | 251. 14.6 22 |
| | | | 386. 25.5 22 |
| | | | 73.7 17.52 22 |
| | | | 312.8 17.25 22 |
| | | | 61.6 14.92 22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING A TWO-TAILED DUNNETT'S TEST

TABLE 7
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN FOOD CONSUMPTION DURING GESTATION (GRAMS/ANIMAL/DAY)

| GROUP : | | 1 | 2 | 3 | 4 |
|------------|--------|--------|--------|--------|--------|
| DAY 0- 6 | MEAN | 22. | 22. | 22. | 23. |
| | S.D./N | 2.4/24 | 2.7/22 | 2.5/24 | 2.6/22 |
| DAY 6- 9 | MEAN | 18. | 19. | 18. | 17. |
| | S.D./N | 2.3/24 | 2.4/22 | 3.5/24 | 3.9/22 |
| DAY 9- 12 | MEAN | 20. | 20. | 20. | 19. |
| | S.D./N | 2.1/24 | 1.9/22 | 2.6/24 | 2.3/22 |
| DAY 12- 16 | MEAN | 22. | 21. | 22. | 22. |
| | S.D./N | 3.0/24 | 2.2/22 | 2.2/24 | 2.9/22 |
| DAY 16- 20 | MEAN | 28. | 28. | 29. | 29. |
| | S.D./N | 2.9/24 | 2.6/22 | 2.4/24 | 2.8/22 |
| DAY 6- 16 | MEAN | 20. | 20. | 20. | 20. |
| | S.D./N | 1.7/24 | 1.9/22 | 2.1/24 | 2.2/22 |
| DAY 0- 20 | MEAN | 22. | 22. | 23. | 22. |
| | S.D./N | 1.9/24 | 1.8/22 | 1.7/24 | 2.1/22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 8
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN FOOD CONSUMPTION DURING GESTATION (GRAMS/KG/DAY)

| GROUP : | | 1 | 2 | 3 | 4 |
|-----------|--------|--------|--------|---------|---------|
| DAY 0-6 | MEAN | 83. | 81. | 82. | 85. |
| | S.D./N | 6.8/24 | 8.5/22 | 8.7/24 | 8.0/22 |
| DAY 6-9 | MEAN | 64. | 67. | 65. | 60. |
| | S.D./N | 6.8/24 | 7.2/22 | 10.6/24 | 11.5/22 |
| DAY 9-12 | MEAN | 67. | 69. | 69. | 67. |
| | S.D./N | 6.2/24 | 5.0/22 | 6.6/24 | 8.0/22 |
| DAY 12-16 | MEAN | 69. | 66. | 69. | 71. |
| | S.D./N | 9.2/24 | 5.3/22 | 6.0/24 | 7.8/22 |
| DAY 16-20 | MEAN | 79. | 78. | 79. | 82. |
| | S.D./N | 6.9/24 | 4.9/22 | 4.7/24 | 7.2/22 |
| DAY 6-16 | MEAN | 68. | 67. | 67. | 66. |
| | S.D./N | 4.1/24 | 4.8/22 | 5.1/24 | 5.6/22 |
| DAY 0-20 | MEAN | 74. | 73. | 74. | 74. |
| | S.D./N | 4.4/24 | 3.5/22 | 4.2/24 | 5.2/22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING A TWO-TAILED DUNNETT'S TEST
 NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 9
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
SUMMARY OF MEAN FETAL DATA AT THE SCHEDULED NECROPSY

| GROUP | SEX | | VIABLE FETUSES | DEAD FETUSES | RESORPTIONS | | POST IMPLANTATION | | PRE IMPLANTATION | | FETAL WEIGHTS IN GRAMS | NO. OF GRAVID FEMALES |
|-------|-----------|------|----------------|--------------|-------------|------|-------------------|-------|------------------|------|------------------------|-----------------------|
| | M | F | | | EARLY | LATE | LOSS | SITES | CORPORA LUTEA | LOSS | | |
| 1 | TOTAL 160 | 141 | 301 | 0 | 21 | 0 | 21 | 322 | 374 | 52 | NA | 24 |
| | MEAN | 6.7 | 5.9 | 0.0 | 0.9 | 0.0 | 0.9 | 13.4 | 15.6 | 2.2 | 3.6 | |
| | S.D. | 3.06 | 2.63 | 0.00 | 1.19 | 0.00 | 1.19 | 4.23 | 3.03 | 2.55 | 0.25 | |
| 2 | TOTAL 159 | 168 | 327 | 0 | 10 | 0 | 10 | 337 | 369 | 32 | NA | 22 |
| | MEAN | 7.2 | 7.6 | 0.0 | 0.5 | 0.0 | 0.5 | 15.3 | 16.8 | 1.5 | 3.4 | |
| | S.D. | 2.91 | 2.52 | 0.00 | 0.86 | 0.00 | 0.86 | 2.38 | 2.39 | 1.34 | 0.18 | |
| 3 | TOTAL 164 | 174 | 338 | 0 | 20 | 0 | 20 | 358 | 423 | 65 | NA | 24 |
| | MEAN | 6.8 | 7.3 | 0.0 | 0.8 | 0.0 | 0.8 | 14.9 | 17.6* | 2.7 | 3.5 | |
| | S.D. | 3.10 | 3.37 | 0.00 | 0.76 | 0.00 | 0.76 | 4.34 | 2.43 | 2.88 | 0.21 | |
| 4 | TOTAL 165 | 139 | 304 | 0 | 24 | 1 | 25 | 329 | 379 | 50 | NA | 22 |
| | MEAN | 7.5 | 6.3 | 0.0 | 1.1 | 0.0 | 1.1 | 15.0 | 17.2 | 2.3 | 3.3** | |
| | S.D. | 2.63 | 2.28 | 0.00 | 1.31 | 0.21 | 1.28 | 3.34 | 3.28 | 2.55 | 0.32 | |

* = SIGNIFICANTLY DIFFERENT FROM CONTROL AT 0.05 LEVEL
** = SIGNIFICANTLY DIFFERENT FROM CONTROL AT 0.01 LEVEL
NA = NOT APPLICABLE

MEAN NUMBER OF VIABLE FETUSES COMPARED USING DUNNETT'S TEST; TOTAL POST IMPLANTATION LOSS COMPARED USING MANN-WHITNEY TEST
TOTAL NUMBER OF DEAD FETUSES COMPARED USING MANN-WHITNEY TEST; MEAN NUMBER OF IMPLANTATION SITES COMPARED USING DUNNETT'S TEST
TOTAL NUMBER OF EARLY RESORPTIONS COMPARED USING MANN-WHITNEY TEST; MEAN NUMBER OF CORPORA LUTEA COMPARED USING DUNNETT'S TEST
TOTAL NUMBER OF LATE RESORPTIONS COMPARED USING MANN-WHITNEY TEST; FETAL WEIGHTS COMPARED USING DUNNETT'S TEST
SEX RATIO COMPARED USING CHI SQUARE TEST

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 10
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SUMMARY OF MEAN FETAL DATA AT SCHEDULED NECROPSY (% PER LITTER)

| GROUP NUMBER: | 1 | 2 | 3 | 4 |
|------------------------------|------|------|-------|------|
| CORPORA LUTEA | | | | |
| MEAN | 15.6 | 16.8 | 17.6* | 17.2 |
| S.D. | 3.03 | 2.39 | 2.43 | 3.28 |
| N | 24 | 22 | 24 | 22 |
| IMPLANTATION SITES | | | | |
| MEAN | 13.4 | 15.3 | 14.9 | 15.0 |
| S.D. | 4.23 | 2.38 | 4.34 | 3.34 |
| N | 24 | 22 | 24 | 22 |
| VIABLE FETUSES (%) | | | | |
| MEAN | 94.2 | 96.8 | 94.8 | 92.6 |
| S.D. | 7.91 | 6.04 | 4.66 | 8.35 |
| N | 24 | 22 | 24 | 22 |
| DEAD FETUSES (%) | | | | |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 |
| S.D. | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 24 | 22 | 24 | 22 |
| EARLY RESORPTIONS (%) | | | | |
| MEAN | 5.8 | 3.2 | 5.2 | 7.1 |
| S.D. | 7.91 | 6.05 | 4.66 | 8.50 |
| N | 24 | 22 | 24 | 22 |
| LATE RESORPTIONS (%) | | | | |
| MEAN | 0.0 | 0.0 | 0.0 | 0.3 |
| S.D. | 0.00 | 0.00 | 0.00 | 1.43 |
| N | 24 | 22 | 24 | 22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

PROPORTIONAL (%) DATA COMPARED USING THE KRUSKAL-WALLIS TEST
 CORPORA LUTEA AND IMPLANTATION SITES COMPARED USING DUNNETT'S TEST
 * = SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP AT THE 0.05 LEVEL

| GROUP NUMBER: | 1 | 2 | 3 | 4 |
|----------------------------|-------|-------|-------|-------|
| TOTAL RESORPTIONS (%) | | | | |
| MEAN | 5.8 | 3.2 | 5.2 | 7.4 |
| S.D. | 7.91 | 6.05 | 4.66 | 8.36 |
| N | 24 | 22 | 24 | 22 |
| PRE-IMPLANTATION LOSS (%) | | | | |
| MEAN | 15.8 | 8.6 | 16.8 | 13.4 |
| S.D. | 24.24 | 7.85 | 20.10 | 17.68 |
| N | 24 | 22 | 24 | 22 |
| POST-IMPLANTATION LOSS (%) | | | | |
| MEAN | 5.8 | 3.2 | 5.2 | 7.4 |
| S.D. | 7.91 | 6.05 | 4.66 | 8.36 |
| N | 24 | 22 | 24 | 22 |
| 45 MALES (%) | | | | |
| MEAN | 52.5 | 48.0 | 49.7 | 55.5 |
| S.D. | 20.70 | 15.51 | 17.39 | 16.16 |
| N | 24 | 22 | 24 | 22 |
| FEMALES (%) | | | | |
| MEAN | 47.5 | 52.0 | 50.3 | 44.5 |
| S.D. | 20.70 | 15.50 | 17.39 | 16.17 |
| N | 24 | 22 | 24 | 22 |
| MALE FETAL WEIGHTS (g) | | | | |
| MEAN | 3.7 | 3.5 | 3.6 | 3.4** |
| S.D. | 0.20 | 0.21 | 0.21 | 0.32 |
| N | 23 | 22 | 24 | 22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

PROPORTIONAL (%) DATA COMPARED USING THE KRUSKAL-WALLIS TEST
 FETAL WEIGHTS COMPARED USING DUNNETT'S TEST

** = SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP AT THE 0.01 LEVEL

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 10
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SUMMARY OF MEAN FETAL DATA AT SCHEDULED NECROPSY (% PER LITTER)

| GROUP NUMBER: | 1 | 2 | 3 | 4 |
|-----------------------------------|------|------|------|-------|
| FEMALE FETAL WEIGHTS (g) | | | | |
| MEAN | 3.4 | 3.3 | 3.4 | 3.2** |
| S.D. | 0.28 | 0.16 | 0.24 | 0.26 |
| N | 23 | 22 | 24 | 21 |
| COMBINED FETAL WEIGHTS (g) | | | | |
| MEAN | 3.6 | 3.4 | 3.5 | 3.3** |
| S.D. | 0.25 | 0.18 | 0.21 | 0.32 |
| N | 24 | 22 | 24 | 22 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

FETAL WEIGHTS COMPARED USING DUNNETT'S TEST

** = SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP AT THE 0.01 LEVEL

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 11
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 NUMBER OF FETUSES AND LITTERS WITH MALFORMATIONS - SUMMARY

PAGE 1
 DAY 20

| | DOSE GROUP: | | | | FETUSES | | | | LITTERS | | | |
|--|-------------|-----|-----|-----|---------|----|----|----|---------|----|----|----|
| | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| NUMBER EXAMINED EXTERNALLY | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 | 24 | 22 | 24 | 22 |
| EXENCEPHALY WITH OR WITHOUT OPEN EYELID | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| MICROPHthalmia AND/OR ANOPHTHALMIA | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| FILAMENTOUS TAIL | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| NUMBER EXAMINED VISCERALLY | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 | 24 | 22 | 24 | 22 |
| SITUS INVERSUS | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| HEART AND/OR GREAT VESSEL ANOMALY | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| NUMBER EXAMINED SKELETALLY | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 | 24 | 22 | 24 | 22 |
| VERTEBRAL ANOMALY WITH OR WITHOUT ASSOCIATED RIB ANOMALY | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| TOTAL NUMBER WITH MALFORMATIONS | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| EXTERNAL : | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 |
| SOFT TISSUE : | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| SKELETAL : | 1 | 2 | 0 | 1 | 1 | 2 | 0 | 1 | 1 | 2 | 0 | 1 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

NONE SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP USING FISHER'S EXACT TEST

TABLE 12

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 PERCENT OF FETUSES AND LITTERS WITH MALFORMATIONS - SUMMARY

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| | FETUSES | | | | LITTERS | | | | |
|--|-------------|-----|-----|-----|---------|-----|-----|-----|-----|
| | DOSE GROUP: | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| NUMBER EXAMINED EXTERNALLY | | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 |
| EXENCEPHALY WITH OR WITHOUT OPEN EYELID | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| MICROPHthalmia AND/OR ANOPHTHALMIA | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| FILAMENTOUS TAIL | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| NUMBER EXAMINED VISCERALLY | | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 |
| SITUS INVERSUS | | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 |
| HEART AND/OR GREAT VESSEL ANOMALY | | 0.3 | 0.0 | 0.0 | 0.0 | 4.2 | 0.0 | 0.0 | 0.0 |
| NUMBER EXAMINED SKELETALLY | | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 |
| VERTEBRAL ANOMALY WITH OR WITHOUT ASSOCIATED RIB ANOMALY | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| TOTAL NUMBER WITH MALFORMATIONS | | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 | 9.1 | 0.0 | 0.0 |
| EXTERNAL (PERCENT) : | | 0.3 | 0.0 | 0.0 | 0.3 | 4.2 | 0.0 | 0.0 | 4.5 |
| SOFT TISSUE (PERCENT) : | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| SKELETAL (PERCENT) : | | 0.3 | 0.6 | 0.0 | 0.3 | 4.2 | 9.1 | 0.0 | 4.5 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 13
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF MALFORMATIONS - SUMMARY
 % PER LITTER

PAGE 1

DAY 20

| | DOSE GROUP: | | | |
|---|-------------|-------------|-------------|-------------|
| | 1 | 2 | 3 | 4 |
| NUMBER OF LITTERS EXAMINED EXTERNALLY | 24 | 22 | 24 | 22 |
| EXENCEPHALY WITH OR WITHOUT OPEN EYELID | 0.0 S.D. | 0.4 1.94 | 0.0 0.00 | 0.0 0.00 |
| MICROPHTHALMIA AND/OR ANOPHTHALMIA | 0.0 S.D. | 0.4 1.94 | 0.0 0.00 | 0.0 0.00 |
| FILAMENTOUS TAIL | 0.0 S.D. | 0.3 1.33 | 0.0 0.00 | 0.0 0.00 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

TABLE 13
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF MALFORMATIONS - SUMMARY
 % PER LITTER

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

PAGE 2
 DAY 20

| | DOSE GROUP: | | | |
|---------------------------------------|-------------|------|------|------|
| | 1 | 2 | 3 | 4 |
| NUMBER OF LITTERS EXAMINED VISCERALLY | 24 | 22 | 24 | 22 |
| SITUS INVERSUS | 0.0 | 0.0 | 0.0 | 0.3 |
| S.D. | 0.00 | 0.00 | 0.00 | 1.52 |
| HEART AND/OR GREAT VESSEL ANOMALY | 0.3 | 0.0 | 0.0 | 0.0 |
| S.D. | 1.46 | 0.00 | 0.00 | 0.00 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 13
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF MALFORMATIONS - SUMMARY
 % PER LITTER

PAGE 3
 DAY 20

| | | DOSE GROUP: | | | |
|--|-----------------|------------------|-------------------|------|------|
| | | 1 | 2 | 3 | 4 |
| NUMBER OF LITTERS EXAMINED SKELETALLY | | 24 | 22 | 24 | 22 |
| VERTEBRAL ANOMALY WITH OR WITHOUT ASSOCIATED RIB ANOMALY | | 0.0 | 0.4 | 0.0 | 0.0 |
| | S.D. | 0.00 | 1.94 | 0.00 | 0.00 |
| 1- 0 MG/KG/DAY | 2- 30 MG/KG/DAY | 3- 300 MG/KG/DAY | 4- 1000 MG/KG/DAY | | |
| NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST | | | | | |

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL

TABLE 13
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF MALFORMATIONS - SUMMARY
 % PER LITTER

PAGE 4
 DAY 20

| | DOSE GROUP: | | | |
|---|-------------|------|------|------|
| | 1 | 2 | 3 | 4 |
| NUMBER OF LITTERS EXAMINED | 24 | 22 | 24 | 22 |
| TOTAL MALFORMATIONS | | | | |
| PERCENT PER LITTER WITH EXTERNAL MALFORMATIONS | 0.0 | 0.7 | 0.0 | 0.0 |
| S.D. | 0.00 | 2.30 | 0.00 | 0.00 |
| PERCENT PER LITTER WITH SOFT TISSUE MALFORMATIONS | 0.3 | 0.0 | 0.0 | 0.3 |
| S.D. | 1.46 | 0.00 | 0.00 | 1.52 |
| PERCENT PER LITTER WITH SKELETAL MALFORMATIONS | 0.0 | 0.4 | 0.0 | 0.0 |
| S.D. | 0.00 | 1.94 | 0.00 | 0.00 |
| TOTAL PERCENT PER LITTER WITH MALFORMATIONS | 0.3 | 0.7 | 0.0 | 0.3 |
| S.D. | 1.46 | 2.30 | 0.00 | 1.52 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

TABLE 14
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 NUMBER OF FETUSES AND LITTERS WITH VARIATIONS - SUMMARY

| | DOSE GROUP: | | | | FETUSES | | | | LITTERS | | | |
|---|-------------|-----|-----|-----|---------|----|----|----|---------|----|----|----|
| | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| NUMBER EXAMINED EXTERNALLY | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 | 24 | 22 | 24 | 22 |
| NUMBER WITH FINDINGS | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NUMBER EXAMINED VISCERALLY | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 | 24 | 22 | 24 | 22 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 |
| NUMBER EXAMINED SKELETALLY | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 | 24 | 22 | 24 | 22 |
| CERVICAL CENTRUM #1 OSSIFIED | 61 | 49 | 63 | 31 | 18 | 16 | 14 | 12 | 18 | 16 | 14 | 12 |
| 7TH CERVICAL RIB(S) | 3 | 3 | 3 | 5 | 3 | 3 | 3 | 5 | 3 | 3 | 3 | 5 |
| STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | 26 | 24 | 22 | 26 | 11 | 10 | 9 | 13 | 11 | 10 | 9 | 13 |
| STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED | 0 | 2 | 2 | 1 | 0 | 2 | 2 | 1 | 0 | 2 | 2 | 1 |
| BENT RIB(S) | 1 | 2 | 1 | 5 | 1 | 1 | 1 | 3 | 1 | 1 | 1 | 3 |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 14 | 14 | 12 | 1 | 8 | 5 | 4 | 1* | 8 | 5 | 4 | 1* |
| 14TH RUDIMENTARY RIB(S) | 0 | 3 | 9 | 10 | 0 | 2 | 6* | 6* | 0 | 2 | 6* | 6* |
| HYOID UNOSSIFIED | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 14TH FULL RIB(S) | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| 25 PRESACRAL VERTEBRAE | 2 | 1 | 0 | 0 | 2 | 1 | 0 | 0 | 2 | 1 | 0 | 0 |
| PUBIS UNOSSIFIED | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| STERNEBRA(E) MALALIGNED (SLIGHT OR MODERATE) | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

* = SIGNIFICANTLY DIFFERENT FROM THE CONTROL GROUP AT THE 0.05 LEVEL USING FISHER'S EXACT TEST

TABLE 15

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 PERCENT OF FETUSES AND LITTERS WITH VARIATIONS - SUMMARY

| | FETUSES | | | | LITTERS | | | | |
|---|-----------------|------------------|-------------------|------|---------|------|------|------|------|
| | DOSE GROUP: | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| NUMBER EXAMINED EXTERNALLY | | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 |
| NUMBER WITH FINDINGS | | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| NUMBER EXAMINED VISCERALLY | | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | | 0.0 | 0.3 | 0.3 | 0.3 | 0.0 | 4.5 | 4.2 | 4.5 |
| NUMBER EXAMINED SKELETALLY | | 301 | 327 | 338 | 304 | 24 | 22 | 24 | 22 |
| CERVICAL CENTRUM #1 OSSIFIED | | 20.3 | 15.0 | 18.6 | 10.2 | 75.0 | 72.7 | 58.3 | 54.5 |
| 7TH CERVICAL RIB(S) | | 1.0 | 0.9 | 0.9 | 1.6 | 12.5 | 13.6 | 12.5 | 22.7 |
| STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | | 8.6 | 7.3 | 6.5 | 8.6 | 45.8 | 45.5 | 37.5 | 59.1 |
| STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED | | 0.0 | 0.6 | 0.6 | 0.3 | 0.0 | 9.1 | 8.3 | 4.5 |
| BENT RIB(S) | | 0.3 | 0.6 | 0.3 | 1.6 | 4.2 | 4.5 | 4.2 | 13.6 |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | | 4.7 | 4.3 | 3.6 | 0.3 | 33.3 | 22.7 | 16.7 | 4.5 |
| 14TH RUDIMENTARY RIB(S) | | 0.0 | 0.9 | 2.7 | 3.3 | 0.0 | 9.1 | 25.0 | 27.3 |
| HYOID UNOSSIFIED | | 0.3 | 0.0 | 0.0 | 0.0 | 4.2 | 0.0 | 0.0 | 0.0 |
| 14TH FULL RIB(S) | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| 25 PRESACRAL VERTEBRAE | | 0.7 | 0.3 | 0.0 | 0.0 | 8.3 | 4.5 | 0.0 | 0.0 |
| PUBIS UNOSSIFIED | | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 4.5 | 0.0 | 0.0 |
| STERNEBRA(E) MALALIGNED (SLIGHT OR MODERATE) | | 0.0 | 0.3 | 0.3 | 0.3 | 0.0 | 4.5 | 4.2 | 4.5 |
| 1- 0 MG/KG/DAY | 2- 30 MG/KG/DAY | 3- 300 MG/KG/DAY | 4- 1000 MG/KG/DAY | | | | | | |

TABLE 16

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF VARIATIONS - SUMMARY
 % PER LITTER

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

PAGE 1
 DAY 20

| | 1 | 2 | 3 | 4 |
|---------------------------------------|----|----|----|----|
| DOSE GROUP: | | | | |
| NUMBER OF LITTERS EXAMINED EXTERNALLY | 24 | 22 | 24 | 22 |
| NUMBER OF LITTERS WITH FINDINGS | 0 | 0 | 0 | 0 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 16
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF VARIATIONS - SUMMARY
 % PER LITTER

| | DOSE GROUP: | | | | PAGE |
|---|-------------|------|------|------|------|
| | 1 | 2 | 3 | 4 | |
| NUMBER OF LITTERS EXAMINED VISCERALLY | 24 | 22 | 24 | 22 | 2 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 0.0 | 0.5 | 0.3 | 0.3 | 0.3 |
| S.D. | 0.00 | 2.13 | 1.57 | 1.52 | 1.52 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 16
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF VARIATIONS - SUMMARY
 % PER LITTER

PAGE 3

DAY 20

| NUMBER OF LITTERS EXAMINED SKELETALLY | DOSE GROUP: | | | |
|--|-------------|-------|-------|-------|
| | 1 | 2 | 3 | 4 |
| CERVICAL CENTRUM #1 OSSIFIED | 24 | 22 | 24 | 22 |
| | 18.0 | 15.6 | 17.1 | 10.0 |
| | S.D. | 16.61 | 21.95 | 13.21 |
| 7TH CERVICAL RIB(S) | 1.2 | 0.9 | 0.8 | 1.5 |
| | S.D. | 2.31 | 2.25 | 2.86 |
| STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | 8.4 | 7.0 | 5.7 | 8.6 |
| | S.D. | 12.17 | 11.47 | 9.57 |
| STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED | 0.0 | 0.6 | 0.6 | 0.3 |
| | S.D. | 0.00 | 1.90 | 1.25 |
| BENT RIB(S) | 0.3 | 0.6 | 0.3 | 1.8 |
| | S.D. | 1.57 | 1.46 | 5.34 |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 4.9 | 3.9 | 4.0 | 0.3 |
| | S.D. | 10.11 | 11.39 | 1.33 |
| 14TH RUDIMENTARY RIB(S) | 0.0 | 0.9 | 2.4 | 3.4 |
| | S.D. | 0.00 | 5.76 | 6.76 |
| HYOID UNOSSIFIED | 0.3 | 0.0 | 0.0 | 0.0 |
| | S.D. | 1.57 | 0.00 | 0.00 |
| 14TH FULL RIB(S) | 0.0 | 0.3 | 0.0 | 0.0 |
| | S.D. | 0.00 | 0.00 | 0.00 |
| 25 PRESACRAL VERTEBRAE | 0.8 | 0.3 | 0.0 | 0.0 |
| | S.D. | 2.82 | 0.00 | 0.00 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 16
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF VARIATIONS - SUMMARY

PAGE 4
 DAY 20

| | | DOSE GROUP: | | | |
|---|------|-------------|------|------|------|
| | | 1 | 2 | 3 | 4 |
| NUMBER OF LITTERS EXAMINED SKELETALLY | | 24 | 22 | 24 | 22 |
| PUBIS UNOSSIFIED | | 0.0 | 0.3 | 0.0 | 0.0 |
| | S.D. | 0.00 | 1.33 | 0.00 | 0.00 |
| STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) | | 0.0 | 0.5 | 0.3 | 0.3 |
| | S.D. | 0.00 | 2.13 | 1.36 | 1.64 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

TABLE 16

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 MEAN LITTER PROPORTIONS OF VARIATIONS - SUMMARY
 % PER LITTER

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| | DOSE GROUP: | | | |
|--|--------------------|---------------|---------------|---------------|
| | 1 | 2 | 3 | 4 |
| NUMBER OF LITTERS EXAMINED | 24 | 22 | 24 | 22 |
| TOTAL VARIATIONS | | | | |
| PERCENT PER LITTER WITH EXTERNAL VARIATIONS | 0.0 S.D. 0.00 | 0.0 0.00 | 0.0 0.00 | 0.0 0.00 |
| PERCENT PER LITTER WITH SOFT TISSUE VARIATIONS | 0.0 S.D. 0.00 | 0.5 2.13 | 0.3 1.57 | 0.3 1.52 |
| PERCENT PER LITTER WITH SKELETAL VARIATIONS | 30.3 S.D. 19.00 | 26.7 17.54 | 27.9 25.89 | 23.7 17.66 |
| TOTAL PERCENT PER LITTER WITH VARIATIONS | 30.3 S.D. 19.00 | 26.7 17.54 | 28.2 25.68 | 24.1 17.68 |

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY
 NONE SIGNIFICANTLY DIFFERENT USING THE MANN-WHITNEY U TEST

TABLE 17
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | | | | | | | | | | | | | | | | | | | |
|--------------------------------------|--------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| NO SIGNIFICANT CLINICAL OBSERVATIONS | | | | | | | | | | | | | | | | | | | | | |
| 29601 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29609 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29615 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29628 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29634 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29640 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29652 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29661 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29593 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29602 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29639 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29662 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29684 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29623 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29647 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29669 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29683 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29599 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29619 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29644 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29660 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29696 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29709 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29674 | 1 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29603 | 2 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29610 | 2 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |
| 29617 | 2 | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P | P |

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE
 1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | | | | | | | | | | | | | | | | |
|-------------|--------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 1 | 1 | 1 | 2 |
| 29593 | 1 | | | | | | | | | | | | | | | | | P |
| 29602 | 1 | | | | | | | | | | | | | | | | | P |
| 29639 | 1 | | | | | | | | | | | | | | | | | P |
| 29662 | 1 | | | | | | | | | | | | | | | | | P |
| 29684 | 1 | | | | | | | | | | | | | | | | | P |
| 29695 | 1 | | | | | | | | | | | | | | | | | P |
| 29623 | 1 | | | | | | | | | | | | | | | | | P |
| 29647 | 1 | | | | | | | | | | | | | | | | | P |
| 29669 | 1 | | | | | | | | | | | | | | | | | P |
| 29683 | 1 | | | | | | | | | | | | | | | | | P |
| 29599 | 1 | | | | | | | | | | | | | | | | | P |
| 29619 | 1 | | | | | | | | | | | | | | | | | P |
| 29644 | 1 | | | | | | | | | | | | | | | | | P |
| 29660 | 1 | | | | | | | | | | | | | | | | | P |
| 29696 | 1 | | | | | | | | | | | | | | | | | P |
| 29709 | 1 | | | | | | | | | | | | | | | | | P |
| 29674 | 1 | | | | | | | | | | | | | | | | | P |
| 29603 | 2 | | | | | | | | | | | | | | | | | P |
| 29610 | 2 | | | | | | | | | | | | | | | | | P |
| 29617 | 2 | | | | | | | | | | | | | | | | | P |
| 29630 | 2 | | | | | | | | | | | | | | | | | P |
| 29635 | 2 | | | | | | | | | | | | | | | | | P |
| 29645 | 2 | | | | | | | | | | | | | | | | | P |
| 29653 | 2 | | | | | | | | | | | | | | | | | P |
| 29667 | 2 | | | | | | | | | | | | | | | | | P |

SENT TO NECROPSY FOR SCHEDULED LAPAROHYSTERECTOMY;
 GESTATION DAY 20

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | |
|-------------|--------------|-----------------|---|
| | | 0 | 1 |
| | | 1 | 1 |
| | | 2 | 1 |
| | | 3 | 1 |
| | | 4 | 1 |
| | | 5 | 1 |
| | | 6 | 1 |
| | | 7 | 1 |
| | | 8 | 1 |
| | | 9 | 1 |
| | | 10 | 1 |
| | | 11 | 1 |
| | | 12 | 1 |
| | | 13 | 4 |
| | | 14 | 5 |
| | | 15 | 6 |
| | | 16 | 7 |
| | | 17 | 8 |
| | | 18 | 9 |
| | | 19 | 0 |
| | | 20 | 0 |
| | | 21 | 0 |
| | | 22 | 0 |
| | | 23 | 0 |
| | | 24 | 0 |
| | | 25 | 0 |
| | | 26 | 0 |
| | | 27 | 0 |
| | | 28 | 0 |
| | | 29 | 0 |
| | | 30 | 0 |
| | | 31 | 0 |
| | | 32 | 0 |
| | | 33 | 0 |
| | | 34 | 0 |
| | | 35 | 0 |
| | | 36 | 0 |
| | | 37 | 0 |
| | | 38 | 0 |
| | | 39 | 0 |
| | | 40 | 0 |
| | | 41 | 0 |
| | | 42 | 0 |
| | | 43 | 0 |
| | | 44 | 0 |
| | | 45 | 0 |
| | | 46 | 0 |
| | | 47 | 0 |
| | | 48 | 0 |
| | | 49 | 0 |
| | | 50 | 0 |
| | | 51 | 0 |
| | | 52 | 0 |
| | | 53 | 0 |
| | | 54 | 0 |
| | | 55 | 0 |
| | | 56 | 0 |
| | | 57 | 0 |
| | | 58 | 0 |
| | | 59 | 0 |
| | | 60 | 0 |
| | | 61 | 0 |
| | | 62 | 0 |
| | | 63 | 0 |
| | | 64 | 0 |
| | | 65 | 0 |
| | | 66 | 0 |
| | | 67 | 0 |
| | | 68 | 0 |
| | | 69 | 0 |
| | | 70 | 0 |
| | | 71 | 0 |
| | | 72 | 0 |
| | | 73 | 0 |
| | | 74 | 0 |
| | | 75 | 0 |
| | | 76 | 0 |
| | | 77 | 0 |
| | | 78 | 0 |
| | | 79 | 0 |
| | | 80 | 0 |
| | | 81 | 0 |
| | | 82 | 0 |
| | | 83 | 0 |
| | | 84 | 0 |
| | | 85 | 0 |
| | | 86 | 0 |
| | | 87 | 0 |
| | | 88 | 0 |
| | | 89 | 0 |
| | | 90 | 0 |
| | | 91 | 0 |
| | | 92 | 0 |
| | | 93 | 0 |
| | | 94 | 0 |
| | | 95 | 0 |
| | | 96 | 0 |
| | | 97 | 0 |
| | | 98 | 0 |
| | | 99 | 0 |
| | | 100 | 0 |

SENT TO NECROPSY FOR SCHEDULED LAPAROHYSTERECTOMY;
 GESTATION DAY 20

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

OBSERVATION
 ANIMAL GROUP 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0
 GESTATIONAL DAY 1 2

SENT TO NECROPSY FOR SCHEDULED LAPAROHYSTERECTOMY;
 GESTATION DAY 20

| | | |
|-------|---|---|
| 29596 | 3 | P |
| 29620 | 3 | P |
| 29649 | 3 | P |
| 29672 | 3 | P |
| 29688 | 3 | P |
| 29612 | 3 | P |
| 29637 | 3 | P |
| 29664 | 3 | P |
| 29676 | 3 | P |
| 29592 | 3 | P |
| 29614 | 3 | P |
| 29625 | 3 | P |
| 29650 | 3 | P |
| 29677 | 3 | P |
| 29700 | 3 | P |
| 29629 | 3 | P |
| 29678 | 3 | P |
| 29608 | 4 | P |
| 29613 | 4 | P |
| 29626 | 4 | P |
| 29632 | 4 | P |
| 29638 | 4 | P |
| 29651 | 4 | P |
| 29659 | 4 | P |
| 29671 | 4 | P |

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | |
|--|--------------------------|-----------------|---|---|---|---|---|---|---|---|---|----|----|----|---|
| SENT TO NECROPSY FOR SCHEDULED LAPAROHYSTERECTOMY; GESTATION DAY 20 | 29597 | 4 | | | | | | | | | | | | | P |
| | 29621 | 4 | | | | | | | | | | | | | P |
| | 29658 | 4 | | | | | | | | | | | | | P |
| | 29679 | 4 | | | | | | | | | | | | | P |
| | 29694 | 4 | | | | | | | | | | | | | P |
| | 29618 | 4 | | | | | | | | | | | | | P |
| | 29641 | 4 | | | | | | | | | | | | | P |
| | 29665 | 4 | | | | | | | | | | | | | P |
| | 29682 | 4 | | | | | | | | | | | | | P |
| | 29598 | 4 | | | | | | | | | | | | | P |
| | 29616 | 4 | | | | | | | | | | | | | P |
| | 29643 | 4 | | | | | | | | | | | | | P |
| | 29654 | 4 | | | | | | | | | | | | | P |
| | 29681 | 4 | | | | | | | | | | | | | P |
| | 29704 | 4 | | | | | | | | | | | | | P |
| | 29655 | 4 | | | | | | | | | | | | | P |
| | 29680 | 4 | | | | | | | | | | | | | P |
| | HAIR LOSS RIGHT FORELIMB | 29615 | 1 | | | | | | | | | | | | |
| 29661 | | 1 | | | | | | | | | | | 1 | 1 | 1 |
| 29593 | | 1 | | | | | | | | | | | | | 1 |
| 29602 | | 1 | | | | | | | | | | | 1 | 1 | 1 |
| 29662 | | 1 | | | | | | | | | | | | | 1 |
| 29695 | | 1 | | | | | | | | | | | 1 | 1 | 1 |
| 29683 | | 1 | | | | | | | | | | | 1 | 2 | 2 |
| | | | | | | | | | | | | | | | |

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17
 PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | | | | | | | | | | | | | | | | | | |
|--------------------------|--------------|-----------------|---|---|---|---|---|---|---|---|---|----|----|----|---|---|---|---|---|---|
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | | | | | | |
| HAIR LOSS RIGHT FORELIMB | 29681 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | |
| HAIR LOSS LEFT FORELIMB | 29615 | 1 | 1 | 1 | 1 | 1 | | | | | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | |
| | 29661 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | |
| | 29593 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | |
| | 29602 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | |
| | 29695 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | |
| | 29683 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 2 | |
| | 29599 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| | 29644 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| | 29674 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| | 29653 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| | 29667 | 2 | 1 | | | | | | | | | | | | | | | | 1 | |
| | 29605 | 2 | 2 | | | | | | | | | | | | | 1 | 1 | 1 | 1 | |
| | 29633 | 2 | 2 | | | | | | | | | | | | | 1 | 1 | 1 | 1 | |
| | 29600 | 2 | 2 | | | | | | | | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 2 | 2 |
| | 29607 | 3 | 3 | | | | | | | | | | | | | | | | 1 | |
| | 29636 | 3 | 3 | | | | | | | | | | | | | 1 | 1 | 1 | 1 | 1 |
| | 29657 | 3 | 3 | | | | | | | | | | | | | 1 | 1 | 1 | 1 | 1 |
| 29670 | 3 | 3 | | | | | | | | | | | | | 1 | 1 | 1 | 1 | 1 | |
| 29649 | 3 | 3 | | | | | | | | | | | | | 1 | 1 | 2 | 2 | 2 | |
| 29612 | 3 | 3 | | | | | | | | | | | | | | | | 1 | 1 | |
| 29650 | 3 | 3 | | | | | | | | | | | | | 1 | 1 | 1 | 1 | 1 | |
| 29678 | 3 | 3 | | | | | | | | | | | | | 1 | 2 | 2 | 2 | 2 | |
| 29651 | 4 | 4 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 2 | 2 | 2 | |
| 29659 | 4 | 4 | | | | | | | | | | | | | | | | | 1 | 1 |
| 29671 | 4 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE
 1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
SPONSOR: VELSICOL

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | | | | | | | | | | | | | | | | | | |
|------------------------------------|--------------|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------------|
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | | | | | | | | | |
| HAIR LOSS LEFT FORELIMB | 29658 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 29679 | 4 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 29598 | 4 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 29681 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| SCABBING RIGHT FORELIMB | 29661 | 1 | | | | | | | | | | | | | | | | | | PP |
| | 29683 | 1 | | | | | | | | | | | | | | | | | | PP |
| | 29650 | 3 | | | | | | | | | | | | | | | | | | P |
| | 29671 | 4 | | | | | | | | | | | | | | | | | | PPPPPP |
| | 29598 | 4 | | | | | | | | | | | | | | | | | | P |
| | 29681 | 4 | | | | | | | | | | | | | | | | | | P |
| SCABBING LEFT FORELIMB | 29661 | 1 | | | | | | | | | | | | | | | | | | PPP |
| | 29599 | 1 | | | | | | | | | | | | | | | | | | P |
| | 29636 | 3 | | | | | | | | | | | | | | | | | | PP |
| | 29650 | 3 | | | | | | | | | | | | | | | | | | P |
| | 29598 | 4 | | | | | | | | | | | | | | | | | | PP |
| WET BROWN STAINING ANOGENITAL AREA | 29645 | 2 | | | | | | | | | | | | | | | | | | 1 |
| | 29670 | 3 | | | | | | | | | | | | | | | | | | 1 |
| | 29671 | 4 | | | | | | | | | | | | | | | | | | 1 |
| | 29658 | 4 | | | | | | | | | | | | | | | | | | 111 |
| HAIR LOSS VENTRAL THORACIC AREA | 29644 | 1 | | | | | | | | | | | | | | | | | | 1 |
| | 29700 | 3 | | | | | | | | | | | | | | | | | | 1 |
| | 29678 | 3 | | | | | | | | | | | | | | | | | | 1111111111 |
| | 29598 | 4 | | | | | | | | | | | | | | | | | | 1 |

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 17
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| OBSERVATION | ANIMAL GROUP | GESTATIONAL DAY | | | | | | | | | | | | | | | | | | | | | | | |
|--|--------------|-----------------|---|---|---|---|---|---|---|---|---|----|----|----|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | | | | | | | | | | | |
| HAIR LOSS VENTRAL ABDOMINAL AREA | 29644 | | | | | | | | | | | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | | |
| | 29600 | | | | | | | | | | | 1 | 1 | | | | | | | | | | 1 | 1 | 1 |
| | 29650 | | | | | | | | | | | | | | | | | | | | | | 1 | | |
| | 29700 | | | | | | | | | | | | | | | | 1 | 1 | 1 | 2 | 1 | 1 | | | |
| | 29678 | | | | | | | | | | | | | | | | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
| 29598 | 4 | | | | | | | | | | | | | | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 29602 | 1 | | | | | | | | | | | | | | | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | |
| HAIR LOSS LEFT LATERAL THORACIC AREA | 29602 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29644 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29600 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29700 | 3 | | | | | | | | | | | | | | | | | | | | | | | |
| | 29598 | 4 | | | | | | | | | | | | | | | | | | | | | | | |
| HAIR LOSS LEFT LATERAL ABDOMINAL AREA | 29602 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29644 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29600 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29700 | 3 | | | | | | | | | | | | | | | | | | | | | | | |
| | 29598 | 4 | | | | | | | | | | | | | | | | | | | | | | | |
| HAIR LOSS RIGHT LATERAL ABDOMINAL AREA | 29602 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29644 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29600 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29710 | 2 | | | | | | | | | | | | | | | | | | | | | | | |
| | 29700 | 3 | | | | | | | | | | | | | | | | | | | | | | | |
| 29678 | 3 | | | | | | | | | | | | | | | | | | | | | | | | |
| HAIR LOSS RIGHT HINDLIMB | 29602 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29644 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29600 | | | | | | | | | | | | | | | | | | | | | | | | |
| | 29700 | 3 | | | | | | | | | | | | | | | | | | | | | | | |
| | 29678 | 3 | | | | | | | | | | | | | | | | | | | | | | | |

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 18 (1-HOUR POST-DOSING)
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL CLINICAL OBSERVATIONS

OBSERVATION

| ANIMAL GROUP | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | |
|-----------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--|
| GESTATIONAL DAY | | | | | | | | | | | | | | | | | | | | |

WET CLEAR STAINING AROUND MOUTH 29626 4 1

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 30 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 19
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAMS FROM GROUP 1: 0 MG/KG/DAY | | | | | | | | | | | | |
|------------------|--------------------------------|------|------|------|------|------|------|------|------|------|------|------|------|
| | DAY 0 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 12 | 11 | 10 | 9 |
| 29593 NG | 261. | 299. | 300. | 303. | 303. | 299. | 299. | 303. | 303. | 302. | 298. | 298. | 298. |
| 29599 G | 255. | 276. | 276. | 276. | 277. | 283. | 283. | 283. | 283. | 288. | 293. | 288. | 293. |
| 29601 G | 261. | 318. | 312. | 318. | 313. | 320. | 320. | 332. | 332. | 341. | 347. | 341. | 347. |
| 29602 G | 250. | 287. | 290. | 289. | 290. | 295. | 295. | 299. | 299. | 305. | 306. | 305. | 306. |
| 29609 G | 244. | 280. | 274. | 281. | 280. | 282. | 282. | 285. | 285. | 290. | 298. | 290. | 298. |
| 29615 G | 246. | 272. | 261. | 267. | 275. | 273. | 273. | 284. | 284. | 291. | 294. | 291. | 294. |
| 29619 G | 257. | 303. | 301. | 298. | 306. | 314. | 314. | 314. | 314. | 318. | 327. | 318. | 327. |
| 29623 G | 255. | 277. | 274. | 277. | 281. | 291. | 291. | 301. | 301. | 300. | 306. | 300. | 306. |
| 29628 G | 248. | 284. | 283. | 287. | 295. | 297. | 297. | 299. | 299. | 313. | 320. | 313. | 320. |
| 29634 G | 251. | 264. | 271. | 278. | 281. | 288. | 288. | 290. | 290. | 298. | 306. | 298. | 306. |
| 29639 G | 248. | 279. | 276. | 279. | 280. | 285. | 285. | 295. | 295. | 298. | 299. | 298. | 299. |
| 29640 G | 253. | 279. | 281. | 286. | 287. | 290. | 290. | 292. | 292. | 302. | 306. | 302. | 306. |
| 29644 G | 272. | 312. | 315. | 310. | 306. | 296. | 296. | 296. | 296. | 304. | 299. | 304. | 299. |
| 29647 G | 258. | 287. | 289. | 294. | 291. | 298. | 298. | 306. | 306. | 314. | 321. | 314. | 321. |
| 29652 G | 239. | 271. | 263. | 266. | 281. | 283. | 283. | 285. | 285. | 291. | 296. | 291. | 296. |
| 29660 G | 246. | 277. | 275. | 265. | 277. | 278. | 278. | 283. | 283. | 285. | 294. | 285. | 294. |
| 29661 G | 231. | 270. | 267. | 267. | 264. | 274. | 274. | 275. | 275. | 288. | 292. | 288. | 292. |
| 29662 G | 245. | 262. | 261. | 263. | 266. | 278. | 278. | 282. | 282. | 281. | 288. | 281. | 288. |
| 29669 G | 236. | 281. | 270. | 271. | 276. | 288. | 288. | 297. | 297. | 295. | 303. | 295. | 303. |
| 29674 G | 250. | 277. | 271. | 279. | 289. | 290. | 290. | 291. | 291. | 298. | 295. | 298. | 295. |
| 29683 G | 266. | 270. | 276. | 289. | 283. | 299. | 299. | 305. | 305. | 300. | 306. | 300. | 306. |
| 29684 G | 244. | 282. | 277. | 279. | 279. | 293. | 293. | 294. | 294. | 301. | 304. | 301. | 304. |
| 29695 G | 240. | 262. | 267. | 267. | 271. | 270. | 270. | 275. | 275. | 281. | 282. | 281. | 282. |
| 29696 G | 243. | 266. | 275. | 267. | 279. | 282. | 282. | 288. | 288. | 291. | 298. | 291. | 298. |
| 29709 G | 248. | 279. | 273. | 270. | 277. | 287. | 287. | 291. | 291. | 296. | 298. | 296. | 298. |
| MEAN | 249. | 280. | 278. | 280. | 284. | 289. | 289. | 293. | 293. | 299. | 303. | 299. | 303. |
| S.D. | 9.3 | 14.2 | 14.2 | 14.3 | 12.0 | 11.8 | 11.8 | 12.6 | 12.6 | 13.2 | 13.9 | 13.2 | 13.9 |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

| PREGNANCY STATUS | | DAY 14 | DAY 15 | DAY 16 | DAY 20 |
|--------------------------------|----|--------|--------|--------|--------------------------------|
| DAMS FROM GROUP 1: 0 MG/KG/DAY | | | | | |
| 29593 | NG | 305. | 306. | 301. | 305. SCHEDULED NECROPSY DAY 20 |
| 29599 | G | 299. | 303. | 322. | 384. SCHEDULED NECROPSY DAY 20 |
| 29601 | G | 355. | 362. | 383. | 449. SCHEDULED NECROPSY DAY 20 |
| 29602 | G | 310. | 316. | 329. | 391. SCHEDULED NECROPSY DAY 20 |
| 29609 | G | 299. | 301. | 302. | 315. SCHEDULED NECROPSY DAY 20 |
| 29615 | G | 302. | 309. | 316. | 379. SCHEDULED NECROPSY DAY 20 |
| 29619 | G | 327. | 340. | 346. | 411. SCHEDULED NECROPSY DAY 20 |
| 29623 | G | 316. | 318. | 332. | 394. SCHEDULED NECROPSY DAY 20 |
| 29628 | G | 329. | 338. | 350. | 409. SCHEDULED NECROPSY DAY 20 |
| 29634 | G | 305. | 310. | 318. | 389. SCHEDULED NECROPSY DAY 20 |
| 29639 | G | 306. | 313. | 323. | 385. SCHEDULED NECROPSY DAY 20 |
| 29640 | G | 305. | 311. | 321. | 368. SCHEDULED NECROPSY DAY 20 |
| 29644 | G | 300. | 325. | 334. | 394. SCHEDULED NECROPSY DAY 20 |
| 29647 | G | 324. | 332. | 345. | 409. SCHEDULED NECROPSY DAY 20 |
| 29652 | G | 296. | 299. | 303. | 325. SCHEDULED NECROPSY DAY 20 |
| 29660 | G | 303. | 315. | 325. | 381. SCHEDULED NECROPSY DAY 20 |
| 29661 | G | 298. | 304. | 314. | 367. SCHEDULED NECROPSY DAY 20 |
| 29662 | G | 303. | 308. | 320. | 376. SCHEDULED NECROPSY DAY 20 |
| 29669 | G | 312. | 313. | 327. | 383. SCHEDULED NECROPSY DAY 20 |
| 29674 | G | 307. | 317. | 326. | 374. SCHEDULED NECROPSY DAY 20 |
| 29683 | G | 311. | 325. | 332. | 381. SCHEDULED NECROPSY DAY 20 |
| 29684 | G | 308. | 313. | 323. | 370. SCHEDULED NECROPSY DAY 20 |
| 29695 | G | 286. | 298. | 312. | 370. SCHEDULED NECROPSY DAY 20 |
| 29696 | G | 300. | 315. | 326. | 385. SCHEDULED NECROPSY DAY 20 |
| 29709 | G | 296. | 306. | 312. | 359. SCHEDULED NECROPSY DAY 20 |
| MEAN | | 308. | 316. | 327. | 381. |
| S.D. | | 14.2 | 14.8 | 17.0 | 26.6 |
| N | | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 19
 PROJECT NO.: WIL-15218 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSIOOL INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAY 0 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | |
|------------------|-------|------|------|------|------|------|------|------|------|---------------------------------|
| | | | | | | | | | | DAMS FROM GROUP 2: 30 MG/KG/DAY |
| 29591 | G | 253. | 287. | 286. | 291. | 297. | 304. | 310. | 311. | 318. |
| 29595 | G | 250. | 271. | 282. | 276. | 281. | 285. | 289. | 294. | 299. |
| 29600 | G | 257. | 273. | 271. | 271. | 273. | 283. | 287. | 298. | 302. |
| 29603 | NG | 252. | 265. | 262. | 253. | 252. | 263. | 266. | 265. | 261. |
| 29605 | G | 247. | 275. | 277. | 275. | 286. | 288. | 294. | 292. | 298. |
| 29606 | G | 271. | 305. | 300. | 305. | 310. | 317. | 327. | 332. | 336. |
| 29610 | G | 256. | 276. | 277. | 279. | 282. | 285. | 292. | 300. | 300. |
| 29617 | G | 227. | 256. | 253. | 257. | 260. | 267. | 264. | 265. | 266. |
| 29624 | G | 252. | 269. | 269. | 278. | 271. | 285. | 291. | 291. | 300. |
| 29630 | G | 252. | 296. | 284. | 288. | 289. | 296. | 300. | 300. | 311. |
| 29633 | G | 261. | 286. | 291. | 289. | 287. | 292. | 299. | 303. | 310. |
| 29635 | G | 249. | 254. | 248. | 263. | 275. | 278. | 277. | 293. | 299. |
| 29642 | G | 245. | 279. | 279. | 281. | 284. | 287. | 299. | 301. | 302. |
| 29645 | NG | 244. | 257. | 260. | 265. | 265. | 267. | 267. | 269. | 262. |
| 29646 | G | 278. | 298. | 308. | 310. | 310. | 314. | 325. | 327. | 332. |
| 29653 | NG | 251. | 282. | 277. | 278. | 277. | 278. | 283. | 270. | 273. |
| 29663 | G | 279. | 307. | 306. | 310. | 308. | 319. | 327. | 333. | 345. |
| 29666 | G | 258. | 292. | 298. | 298. | 303. | 295. | 305. | 315. | 316. |
| 29667 | G | 249. | 273. | 272. | 277. | 282. | 294. | 291. | 301. | 308. |
| 29668 | G | 256. | 273. | 275. | 272. | 274. | 295. | 297. | 311. | 322. |
| 29673 | G | 245. | 288. | 286. | 286. | 293. | 304. | 311. | 317. | 320. |
| 29675 | G | 247. | 278. | 273. | 276. | 283. | 287. | 294. | 298. | 300. |
| 29685 | G | 246. | 267. | 274. | 274. | 274. | 280. | 290. | 289. | 297. |
| 29698 | G | 248. | 274. | 276. | 269. | 279. | 283. | 286. | 296. | 301. |
| 29710 | G | 239. | 268. | 278. | 273. | 280. | 290. | 293. | 295. | 305. |
| MEAN | | 253. | 279. | 280. | 282. | 286. | 292. | 298. | 303. | 309. |
| S.D. | | 11.8 | 14.2 | 14.7 | 14.2 | 13.3 | 12.9 | 15.4 | 15.5 | 16.5 |
| N | | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 19
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAY 14 | DAY 15 | DAY 16 | DAY 20 | | |
|------------------|--------|--------|--------|--------|------|---------------------------------|
| | | | | | | DAMS FROM GROUP 2: 30 MG/KG/DAY |
| 29591 | G | 326. | 335. | 336. | 400. | SCHEDULED NECROPSY DAY 20 |
| 29595 | G | 306. | 310. | 323. | 391. | SCHEDULED NECROPSY DAY 20 |
| 29600 | G | 295. | 314. | 313. | 388. | SCHEDULED NECROPSY DAY 20 |
| 29603 | NG | 265. | 269. | 271. | 273. | SCHEDULED NECROPSY DAY 20 |
| 29605 | G | 298. | 306. | 314. | 363. | SCHEDULED NECROPSY DAY 20 |
| 29606 | G | 342. | 352. | 367. | 427. | SCHEDULED NECROPSY DAY 20 |
| 29610 | G | 310. | 319. | 323. | 388. | SCHEDULED NECROPSY DAY 20 |
| 29617 | G | 268. | 284. | 287. | 331. | SCHEDULED NECROPSY DAY 20 |
| 29624 | G | 307. | 312. | 316. | 396. | SCHEDULED NECROPSY DAY 20 |
| 29630 | G | 317. | 320. | 333. | 391. | SCHEDULED NECROPSY DAY 20 |
| 29633 | G | 309. | 311. | 319. | 381. | SCHEDULED NECROPSY DAY 20 |
| 29635 | G | 300. | 311. | 317. | 378. | SCHEDULED NECROPSY DAY 20 |
| 29642 | G | 309. | 310. | 327. | 370. | SCHEDULED NECROPSY DAY 20 |
| 29645 | NG | 257. | 262. | 261. | 256. | SCHEDULED NECROPSY DAY 20 |
| 29646 | G | 339. | 355. | 360. | 444. | SCHEDULED NECROPSY DAY 20 |
| 29653 | NG | 271. | 280. | 278. | 278. | SCHEDULED NECROPSY DAY 20 |
| 29663 | G | 349. | 361. | 374. | 447. | SCHEDULED NECROPSY DAY 20 |
| 29666 | G | 315. | 319. | 335. | 385. | SCHEDULED NECROPSY DAY 20 |
| 29667 | G | 310. | 315. | 325. | 380. | SCHEDULED NECROPSY DAY 20 |
| 29668 | G | 329. | 333. | 339. | 411. | SCHEDULED NECROPSY DAY 20 |
| 29673 | G | 329. | 338. | 355. | 424. | SCHEDULED NECROPSY DAY 20 |
| 29675 | G | 308. | 299. | 315. | 376. | SCHEDULED NECROPSY DAY 20 |
| 29685 | G | 313. | 319. | 326. | 393. | SCHEDULED NECROPSY DAY 20 |
| 29698 | G | 302. | 305. | 310. | 363. | SCHEDULED NECROPSY DAY 20 |
| 29710 | G | 309. | 319. | 311. | 377. | SCHEDULED NECROPSY DAY 20 |
| MEAN | | 313. | 320. | 328. | 391. | |
| S.D. | | 17.7 | 18.6 | 20.6 | 27.0 | |
| N | | 22 | 22 | 22 | 22 | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 19
 PROJECT NO.: WIL-15218 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSICOL INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAY 0 | DAY 6 | DAY 7 | DAY 8 | DAY 9 | DAY 10 | DAY 11 | DAY 12 | DAY 13 | |
|------------------|-------|-------|-------|-------|-------|--------|--------|--------|--------|----------------------------------|
| | | | | | | | | | | DAMS FROM GROUP 3: 300 MG/KG/DAY |
| G | 29592 | 275. | 286. | 283. | 283. | 288. | 296. | 303. | 303. | 305. |
| G | 29596 | 269. | 312. | 316. | 318. | 324. | 333. | 342. | 354. | 357. |
| G | 29607 | 233. | 277. | 276. | 277. | 283. | 283. | 295. | 305. | 314. |
| G | 29611 | 237. | 268. | 262. | 267. | 272. | 274. | 282. | 280. | 285. |
| G | 29612 | 252. | 275. | 270. | 280. | 279. | 285. | 286. | 281. | 286. |
| G | 29614 | 256. | 303. | 302. | 302. | 310. | 319. | 324. | 327. | 331. |
| G | 29620 | 254. | 281. | 289. | 293. | 289. | 291. | 307. | 322. | 320. |
| G | 29622 | 244. | 291. | 296. | 292. | 299. | 298. | 299. | 309. | 319. |
| G | 29625 | 275. | 290. | 290. | 290. | 298. | 304. | 305. | 312. | 321. |
| G | 29629 | 258. | 285. | 287. | 288. | 300. | 304. | 302. | 317. | 318. |
| G | 29631 | 239. | 269. | 266. | 270. | 278. | 283. | 284. | 283. | 298. |
| G | 29636 | 249. | 276. | 275. | 276. | 285. | 287. | 292. | 305. | 308. |
| G | 29637 | 273. | 279. | 271. | 268. | 274. | 288. | 308. | 298. | 308. |
| G | 29648 | 274. | 300. | 301. | 302. | 305. | 312. | 313. | 322. | 325. |
| G | 29649 | 254. | 288. | 290. | 292. | 297. | 303. | 310. | 314. | 316. |
| G | 29650 | 250. | 271. | 258. | 257. | 262. | 276. | 278. | 277. | 284. |
| G | 29657 | 243. | 273. | 264. | 267. | 269. | 272. | 278. | 283. | 298. |
| G | 29664 | 264. | 280. | 274. | 274. | 277. | 285. | 294. | 297. | 303. |
| G | 29670 | 250. | 278. | 270. | 282. | 281. | 282. | 279. | 299. | 313. |
| NG | 29672 | 239. | 279. | 280. | 278. | 283. | 282. | 289. | 292. | 287. |
| G | 29676 | 254. | 281. | 284. | 283. | 285. | 292. | 305. | 305. | 314. |
| G | 29677 | 277. | 309. | 307. | 308. | 314. | 324. | 327. | 331. | 336. |
| G | 29678 | 261. | 280. | 280. | 283. | 285. | 287. | 295. | 297. | 304. |
| G | 29688 | 243. | 267. | 278. | 276. | 282. | 289. | 295. | 299. | 306. |
| G | 29700 | 255. | 282. | 281. | 275. | 284. | 296. | 296. | 298. | 296. |
| MEAN | | 256. | 283. | 282. | 283. | 288. | 294. | 300. | 305. | 311. |
| S.D. | | 12.9 | 12.3 | 14.9 | 14.4 | 14.9 | 15.6 | 16.0 | 18.3 | 16.8 |
| N | | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 19
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL

| PREGNANCY STATUS | DAY 14 | DAY 15 | DAY 16 | DAY 20 |
|----------------------------------|--------|--------|--------|--------------------------------|
| DAMS FROM GROUP 3: 300 MG/KG/DAY | | | | |
| 29592 G | 322. | 334. | 344. | 413. SCHEDULED NECROPSY DAY 20 |
| 29596 G | 357. | 367. | 384. | 444. SCHEDULED NECROPSY DAY 20 |
| 29607 G | 316. | 326. | 339. | 408. SCHEDULED NECROPSY DAY 20 |
| 29611 G | 290. | 291. | 299. | 324. SCHEDULED NECROPSY DAY 20 |
| 29612 G | 295. | 296. | 302. | 324. SCHEDULED NECROPSY DAY 20 |
| 29614 G | 330. | 347. | 356. | 420. SCHEDULED NECROPSY DAY 20 |
| 29620 G | 326. | 338. | 354. | 398. SCHEDULED NECROPSY DAY 20 |
| 29622 G | 323. | 328. | 338. | 404. SCHEDULED NECROPSY DAY 20 |
| 29625 G | 323. | 337. | 345. | 410. SCHEDULED NECROPSY DAY 20 |
| 29629 G | 326. | 334. | 339. | 389. SCHEDULED NECROPSY DAY 20 |
| 29631 G | 299. | 309. | 321. | 389. SCHEDULED NECROPSY DAY 20 |
| 29636 G | 310. | 321. | 325. | 378. SCHEDULED NECROPSY DAY 20 |
| 29637 G | 324. | 340. | 356. | 438. SCHEDULED NECROPSY DAY 20 |
| 29648 G | 325. | 332. | 334. | 377. SCHEDULED NECROPSY DAY 20 |
| 29649 G | 322. | 327. | 338. | 416. SCHEDULED NECROPSY DAY 20 |
| 29650 G | 301. | 306. | 317. | 381. SCHEDULED NECROPSY DAY 20 |
| 29657 G | 299. | 310. | 316. | 385. SCHEDULED NECROPSY DAY 20 |
| 29664 G | 307. | 318. | 332. | 395. SCHEDULED NECROPSY DAY 20 |
| 29670 G | 314. | 328. | 335. | 407. SCHEDULED NECROPSY DAY 20 |
| 29672 NG | 290. | 284. | 277. | 276. SCHEDULED NECROPSY DAY 20 |
| 29676 G | 320. | 332. | 346. | 417. SCHEDULED NECROPSY DAY 20 |
| 29677 G | 338. | 350. | 362. | 422. SCHEDULED NECROPSY DAY 20 |
| 29678 G | 314. | 325. | 333. | 387. SCHEDULED NECROPSY DAY 20 |
| 29688 G | 309. | 316. | 331. | 397. SCHEDULED NECROPSY DAY 20 |
| 29700 G | 307. | 318. | 329. | 391. SCHEDULED NECROPSY DAY 20 |
| MEAN | 317. | 326. | 336. | 396. |
| S.D. | 14.8 | 17.1 | 18.8 | 28.4 |
| N | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 19
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

PROJECT NO.: WIL-15218
 SPONSOR: VELSITCOOL

| PREGNANCY STATUS | DAY 0 | | | | | | | | | | | | |
|------------------|----------------|------|------|------|------|------|------|------|------|------|--|--|--|
| | 1000 MG/KG/DAY | | | | | | | | | | | | |
| 29597 | G | 234. | 250. | 250. | 227. | 244. | 257. | 269. | 277. | 280. | | | |
| 29598 | G | 263. | 297. | 291. | 296. | 299. | 305. | 303. | 310. | 318. | | | |
| 29608 | G | 246. | 275. | 274. | 277. | 285. | 283. | 287. | 296. | 307. | | | |
| 29613 | G | 233. | 261. | 254. | 254. | 258. | 266. | 267. | 272. | 280. | | | |
| 29616 | G | 252. | 284. | 270. | 274. | 281. | 286. | 293. | 295. | 302. | | | |
| 29618 | G | 264. | 293. | 294. | 289. | 288. | 290. | 299. | 308. | 311. | | | |
| 29621 | G | 250. | 272. | 257. | 279. | 280. | 286. | 293. | 301. | 308. | | | |
| 29626 | G | 247. | 288. | 283. | 287. | 290. | 292. | 299. | 307. | 313. | | | |
| 29632 | G | 240. | 276. | 272. | 277. | 264. | 265. | 276. | 285. | 298. | | | |
| 29638 | G | 250. | 292. | 291. | 289. | 292. | 298. | 297. | 303. | 309. | | | |
| 29641 | G | 257. | 271. | 268. | 265. | 268. | 275. | 295. | 290. | 295. | | | |
| 29643 | G | 278. | 310. | 305. | 297. | 310. | 311. | 309. | 318. | 326. | | | |
| 29651 | G | 252. | 282. | 272. | 272. | 280. | 294. | 294. | 311. | 314. | | | |
| 29654 | NG | 249. | 283. | 286. | 284. | 288. | 299. | 295. | 293. | 286. | | | |
| 29655 | G | 267. | 312. | 303. | 311. | 313. | 311. | 323. | 325. | 337. | | | |
| 29658 | NG | 243. | 250. | 247. | 251. | 250. | 253. | 243. | 244. | 248. | | | |
| 29659 | G | 258. | 284. | 269. | 264. | 273. | 277. | 279. | 276. | 285. | | | |
| 29665 | G | 238. | 274. | 267. | 265. | 271. | 273. | 290. | 296. | 299. | | | |
| 29671 | G | 220. | 266. | 264. | 261. | 259. | 267. | 272. | 271. | 281. | | | |
| 29679 | G | 265. | 291. | 295. | 298. | 293. | 297. | 307. | 314. | 313. | | | |
| 29680 | G | 271. | 300. | 282. | 283. | 300. | 294. | 304. | 306. | 311. | | | |
| 29681 | NG | 271. | 304. | 300. | 291. | 296. | 295. | 296. | 298. | 286. | | | |
| 29682 | G | 229. | 271. | 257. | 240. | 262. | 272. | 284. | 293. | 300. | | | |
| 29694 | G | 260. | 291. | 277. | 287. | 290. | 295. | 302. | 304. | 311. | | | |
| 29704 | G | 251. | 283. | 280. | 280. | 284. | 294. | 300. | 305. | 304. | | | |
| MEAN | | 251. | 283. | 276. | 276. | 281. | 286. | 293. | 298. | 305. | | | |
| S.D. | | 14.6 | 15.2 | 15.6 | 19.5 | 17.5 | 15.1 | 14.0 | 14.9 | 14.5 | | | |
| N | | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 19
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHTS (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAY 14 | DAY 15 | DAY 16 | DAY 20 | DAMS FROM GROUP 4: 1000 MG/KG/DAY |
|------------------|--------|--------|--------|--------|-----------------------------------|
| | | | | | |
| 29597 | G | 279. | 281. | 293. | 341. SCHEDULED NECROPSY DAY 20 |
| 29598 | G | 326. | 327. | 340. | 395. SCHEDULED NECROPSY DAY 20 |
| 29608 | G | 308. | 320. | 328. | 391. SCHEDULED NECROPSY DAY 20 |
| 29613 | G | 281. | 286. | 296. | 351. SCHEDULED NECROPSY DAY 20 |
| 29616 | G | 307. | 319. | 327. | 391. SCHEDULED NECROPSY DAY 20 |
| 29618 | G | 317. | 321. | 333. | 381. SCHEDULED NECROPSY DAY 20 |
| 29621 | G | 309. | 318. | 331. | 401. SCHEDULED NECROPSY DAY 20 |
| 29626 | G | 316. | 323. | 329. | 384. SCHEDULED NECROPSY DAY 20 |
| 29632 | G | 300. | 309. | 317. | 371. SCHEDULED NECROPSY DAY 20 |
| 29638 | G | 311. | 317. | 332. | 394. SCHEDULED NECROPSY DAY 20 |
| 29641 | G | 299. | 314. | 328. | 390. SCHEDULED NECROPSY DAY 20 |
| 29643 | G | 334. | 337. | 357. | 434. SCHEDULED NECROPSY DAY 20 |
| 29651 | G | 317. | 325. | 340. | 418. SCHEDULED NECROPSY DAY 20 |
| 29654 | NG | 294. | 296. | 290. | 295. SCHEDULED NECROPSY DAY 20 |
| 29655 | G | 351. | 355. | 361. | 417. SCHEDULED NECROPSY DAY 20 |
| 29658 | NG | 253. | 251. | 250. | 257. SCHEDULED NECROPSY DAY 20 |
| 29659 | G | 293. | 296. | 300. | 327. SCHEDULED NECROPSY DAY 20 |
| 29665 | G | 300. | 314. | 328. | 373. SCHEDULED NECROPSY DAY 20 |
| 29671 | G | 284. | 292. | 297. | 356. SCHEDULED NECROPSY DAY 20 |
| 29679 | G | 318. | 327. | 339. | 400. SCHEDULED NECROPSY DAY 20 |
| 29680 | G | 312. | 316. | 321. | 385. SCHEDULED NECROPSY DAY 20 |
| 29681 | NG | 296. | 304. | 299. | 300. SCHEDULED NECROPSY DAY 20 |
| 29682 | G | 307. | 316. | 329. | 398. SCHEDULED NECROPSY DAY 20 |
| 29694 | G | 309. | 321. | 330. | 403. SCHEDULED NECROPSY DAY 20 |
| 29704 | G | 313. | 326. | 338. | 401. SCHEDULED NECROPSY DAY 20 |
| MEAN | | 309. | 316. | 327. | 386. |
| S.D. | | 16.6 | 16.4 | 17.8 | 25.5 |
| N | | 22 | 22 | 22 | 22 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 20
 PROJECT NO.: WIL-15218 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSICOL
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAYS | | | | | | | | | | | 13-14 |
|--------------------------------|------|------|------|-----|------|-------|-------|-------|-----|--|--|-------|
| | 0-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | | | | |
| DAMS FROM GROUP 1: 0 MG/KG/DAY | | | | | | | | | | | | |
| 29593 | 38. | 1. | 3. | 0. | -4. | 4. | -1. | -4. | 7. | | | |
| 29599 | 21. | 0. | 0. | 1. | 6. | 0. | 5. | 5. | 6. | | | |
| 29601 | 57. | -6. | 6. | -5. | 7. | 12. | 9. | 6. | 8. | | | |
| 29602 | 37. | 3. | -1. | 1. | 5. | 4. | 6. | 1. | 4. | | | |
| 29609 | 36. | -6. | 7. | -1. | 2. | 3. | 5. | 8. | 1. | | | |
| 29615 | 26. | -11. | 6. | 8. | -2. | 11. | 7. | 3. | 8. | | | |
| 29619 | 46. | -2. | -3. | 8. | 8. | 0. | 4. | 9. | 0. | | | |
| 29623 | 22. | -3. | 3. | 4. | 10. | 10. | -1. | 6. | 10. | | | |
| 29628 | 36. | -1. | 4. | 8. | 2. | 2. | 14. | 7. | 9. | | | |
| 29634 | 13. | 7. | 7. | 3. | 7. | 2. | 8. | 8. | -1. | | | |
| 29639 | 31. | -3. | 3. | 1. | 5. | 10. | 3. | 1. | 7. | | | |
| 29640 | 26. | 2. | 5. | 1. | 3. | 2. | 10. | 4. | -1. | | | |
| 29644 | 40. | 3. | -5. | -4. | -10. | 0. | 8. | -5. | 1. | | | |
| 29647 | 29. | 2. | 5. | -3. | 7. | 8. | 8. | 7. | 3. | | | |
| 29652 | 32. | -8. | 3. | 15. | 2. | 2. | 6. | 5. | 0. | | | |
| 29660 | 31. | -2. | -10. | 12. | 1. | 5. | 2. | 9. | 9. | | | |
| 29661 | 39. | -3. | 0. | -3. | 10. | 1. | 13. | 4. | 6. | | | |
| 29662 | 17. | -1. | 2. | 3. | 12. | 4. | -1. | 7. | 15. | | | |
| 29669 | 45. | -11. | 1. | 5. | 12. | 9. | -2. | 8. | 9. | | | |
| 29674 | 27. | -6. | 8. | 10. | 1. | 1. | 7. | -3. | 12. | | | |
| 29683 | 4. | 6. | 13. | -6. | 16. | 6. | -5. | 6. | 5. | | | |
| 29684 | 38. | -5. | 2. | 0. | 14. | 1. | 7. | 3. | 4. | | | |
| 29695 | 22. | 5. | 0. | 4. | -1. | 5. | 6. | 1. | 4. | | | |
| 29696 | 23. | 9. | -8. | 12. | 3. | 6. | 3. | 7. | 2. | | | |
| 29709 | 31. | -6. | -3. | 7. | 10. | 4. | 5. | 2. | -2. | | | |
| MEAN | 30. | -2. | 2. | 3. | 5. | 5. | 5. | 5. | 5. | | | |
| S.D. | 11.4 | 5.4 | 5.2 | 5.7 | 5.8 | 3.7 | 4.5 | 3.6 | 4.5 | | | |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

UN

TABLE 20
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| PREGNANCY STATUS | DAYS FROM GROUP 1: 0 MG/KG/DAY | | | | | | | SCHEDULED NECROPSY DAY |
|------------------|--------------------------------|-------|-------|-----|------|-------|------|--------------------------------|
| | DAY 14-15 | 15-16 | 16-20 | 6-9 | 9-12 | 12-16 | 6-16 | |
| 29593 NG | 1. | -5. | 4. | 4. | -1. | -1. | 2. | 44. SCHEDULED NECROPSY DAY 20 |
| 29599 G | 4. | 19. | 62. | 1. | 11. | 34. | 46. | 129. SCHEDULED NECROPSY DAY 20 |
| 29601 G | 7. | 21. | 66. | -5. | 28. | 42. | 65. | 188. SCHEDULED NECROPSY DAY 20 |
| 29602 G | 6. | 13. | 62. | 3. | 15. | 24. | 42. | 141. SCHEDULED NECROPSY DAY 20 |
| 29609 G | 2. | 1. | 13. | 0. | 10. | 12. | 22. | 71. SCHEDULED NECROPSY DAY 20 |
| 29615 G | 7. | 7. | 63. | 3. | 16. | 25. | 44. | 133. SCHEDULED NECROPSY DAY 20 |
| 29619 G | 13. | 6. | 65. | 3. | 12. | 28. | 43. | 154. SCHEDULED NECROPSY DAY 20 |
| 29623 G | 2. | 14. | 62. | 4. | 19. | 32. | 55. | 139. SCHEDULED NECROPSY DAY 20 |
| 29628 G | 9. | 12. | 59. | 11. | 18. | 37. | 66. | 161. SCHEDULED NECROPSY DAY 20 |
| 29634 G | 5. | 8. | 71. | 17. | 17. | 20. | 54. | 138. SCHEDULED NECROPSY DAY 20 |
| 29639 G | 7. | 10. | 62. | 1. | 18. | 25. | 44. | 137. SCHEDULED NECROPSY DAY 20 |
| 29640 G | 6. | 10. | 47. | 8. | 15. | 19. | 42. | 115. SCHEDULED NECROPSY DAY 20 |
| 29644 G | 25. | 9. | 60. | -6. | -2. | 30. | 22. | 122. SCHEDULED NECROPSY DAY 20 |
| 29647 G | 8. | 13. | 64. | 4. | 23. | 31. | 58. | 151. SCHEDULED NECROPSY DAY 20 |
| 29652 G | 3. | 4. | 22. | 10. | 10. | 12. | 32. | 86. SCHEDULED NECROPSY DAY 20 |
| 29660 G | 12. | 10. | 56. | 0. | 8. | 40. | 48. | 135. SCHEDULED NECROPSY DAY 20 |
| 29661 G | 6. | 10. | 53. | -6. | 24. | 26. | 44. | 136. SCHEDULED NECROPSY DAY 20 |
| 29662 G | 5. | 12. | 56. | 4. | 15. | 39. | 58. | 131. SCHEDULED NECROPSY DAY 20 |
| 29669 G | 1. | 14. | 56. | -5. | 19. | 32. | 46. | 147. SCHEDULED NECROPSY DAY 20 |
| 29674 G | 10. | 9. | 48. | 12. | 9. | 28. | 49. | 124. SCHEDULED NECROPSY DAY 20 |
| 29683 G | 14. | 7. | 49. | 13. | 17. | 32. | 62. | 115. SCHEDULED NECROPSY DAY 20 |
| 29684 G | 5. | 10. | 47. | -3. | 22. | 22. | 41. | 126. SCHEDULED NECROPSY DAY 20 |
| 29695 G | 12. | 14. | 58. | 9. | 10. | 31. | 50. | 130. SCHEDULED NECROPSY DAY 20 |
| 29696 G | 15. | 11. | 59. | 13. | 12. | 35. | 60. | 142. SCHEDULED NECROPSY DAY 20 |
| 29709 G | 10. | 6. | 47. | -2. | 19. | 16. | 33. | 111. SCHEDULED NECROPSY DAY 20 |
| MEAN | 8. | 10. | 54. | 4. | 15. | 28. | 47. | 132. |
| S.D. | 5.3 | 4.4 | 13.2 | 6.7 | 6.3 | 8.3 | 11.9 | 23.2 |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 20
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| PREGNANCY STATUS | DAYS FROM GROUP 2: 30 MG/KG/DAY | | | | | | | | | | | | | |
|------------------|---------------------------------|------|-----|-----|------|-------|-------|-------|-------|--|--|--|--|--|
| | DAY 0-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | | | | | |
| 29591 G | 34. | -1. | 5. | 6. | 7. | 6. | 1. | 7. | 8. | | | | | |
| 29595 G | 21. | 11. | -6. | 5. | 4. | 4. | 5. | 5. | 7. | | | | | |
| 29600 G | 16. | -2. | 0. | 2. | 10. | 4. | 11. | 4. | 5. | | | | | |
| 29603 NG | 13. | -3. | -9. | -1. | 11. | 3. | -1. | -4. | 4. | | | | | |
| 29605 G | 28. | 2. | -2. | 11. | 2. | 6. | -2. | 6. | 0. | | | | | |
| 29606 G | 34. | -5. | 5. | 5. | 7. | 10. | 5. | 4. | 6. | | | | | |
| 29610 G | 20. | 1. | 2. | 3. | 3. | 7. | 8. | 0. | 10. | | | | | |
| 29617 G | 29. | -3. | 4. | 3. | 7. | -3. | 1. | 1. | 2. | | | | | |
| 29624 G | 17. | 0. | 9. | -7. | 14. | 6. | 0. | 9. | 7. | | | | | |
| 29630 G | 44. | -12. | 4. | 1. | 7. | 4. | 0. | 11. | 6. | | | | | |
| 29633 G | 25. | 5. | -2. | -2. | 5. | 7. | 4. | 7. | -1. | | | | | |
| 29635 G | 5. | -6. | 15. | 12. | 3. | -1. | 16. | 6. | 1. | | | | | |
| 29642 G | 34. | 0. | 2. | 3. | 3. | 12. | 2. | 1. | 7. | | | | | |
| 29645 NG | 13. | 3. | 5. | 0. | 2. | 0. | 2. | -7. | -5. | | | | | |
| 29646 G | 20. | 10. | 2. | 0. | 4. | 11. | 2. | 5. | 7. | | | | | |
| 29653 NG | 31. | -5. | 1. | -1. | 1. | 5. | -13. | 3. | -2. | | | | | |
| 29663 G | 28. | -1. | 4. | -2. | 11. | 8. | 6. | 12. | 4. | | | | | |
| 29666 G | 34. | 6. | 0. | 5. | -8. | 10. | 10. | 1. | -1. | | | | | |
| 29667 G | 24. | -1. | 5. | 5. | 12. | -3. | 10. | 7. | 2. | | | | | |
| 29668 G | 17. | 2. | -3. | 2. | 21. | 2. | 14. | 11. | 7. | | | | | |
| 29673 G | 43. | -2. | 0. | 7. | 11. | 7. | 6. | 3. | 9. | | | | | |
| 29675 G | 31. | -5. | 3. | 7. | 4. | 7. | 4. | 2. | 8. | | | | | |
| 29685 G | 21. | 7. | 0. | 0. | 6. | 10. | -1. | 8. | 16. | | | | | |
| 29698 G | 26. | 2. | -7. | 10. | 4. | 3. | 10. | 5. | 1. | | | | | |
| 29710 G | 29. | 10. | -5. | 7. | 10. | 3. | 2. | 10. | 4. | | | | | |
| MEAN | 26. | 1. | 2. | 4. | 7. | 5. | 5. | 6. | 5. | | | | | |
| S.D. | 9.1 | 5.7 | 5.0 | 4.5 | 5.6 | 4.2 | 5.0 | 3.5 | 4.8 | | | | | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | | | | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

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TABLE 20
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| PREGNANCY STATUS | DAMS FROM GROUP 2: 30 MG/KG/DAY | | | | | | | | | |
|------------------|---------------------------------|-------|-------|------|------|-------|------|------|-----------|-----------------|
| | DAY 14-15 | 15-16 | 16-20 | 6-9 | 9-12 | 12-16 | 6-16 | 0-20 | | |
| 29591 G | 9. | 1. | 64. | 10. | 14. | 25. | 49. | 147. | SCHEDULED | NECROPSY DAY 20 |
| 29595 G | 4. | 13. | 68. | 10. | 13. | 29. | 52. | 141. | SCHEDULED | NECROPSY DAY 20 |
| 29600 G | 19. | -1. | 75. | 0. | 25. | 15. | 40. | 131. | SCHEDULED | NECROPSY DAY 20 |
| 29603 NG | 4. | 2. | 2. | -13. | 13. | 6. | 6. | 21. | SCHEDULED | NECROPSY DAY 20 |
| 29605 G | 8. | 8. | 49. | 11. | 6. | 22. | 39. | 116. | SCHEDULED | NECROPSY DAY 20 |
| 29606 G | 10. | 15. | 60. | 5. | 22. | 35. | 62. | 156. | SCHEDULED | NECROPSY DAY 20 |
| 29610 G | 9. | 4. | 65. | 6. | 18. | 23. | 47. | 132. | SCHEDULED | NECROPSY DAY 20 |
| 29617 G | 16. | 3. | 44. | 4. | 5. | 22. | 31. | 104. | SCHEDULED | NECROPSY DAY 20 |
| 29624 G | 5. | 4. | 80. | 2. | 20. | 25. | 47. | 144. | SCHEDULED | NECROPSY DAY 20 |
| 29630 G | 3. | 13. | 58. | -7. | 11. | 33. | 37. | 139. | SCHEDULED | NECROPSY DAY 20 |
| 29633 G | 2. | 8. | 62. | 1. | 16. | 16. | 33. | 120. | SCHEDULED | NECROPSY DAY 20 |
| 29635 G | 11. | 6. | 61. | 21. | 18. | 24. | 63. | 129. | SCHEDULED | NECROPSY DAY 20 |
| 29642 G | 1. | 17. | 43. | 5. | 17. | 26. | 48. | 125. | SCHEDULED | NECROPSY DAY 20 |
| 29645 NG | 5. | -1. | -5. | 8. | 4. | -8. | 4. | 12. | SCHEDULED | NECROPSY DAY 20 |
| 29646 G | 16. | 5. | 84. | 12. | 17. | 33. | 62. | 166. | SCHEDULED | NECROPSY DAY 20 |
| 29653 NG | 9. | -2. | 0. | -5. | -7. | 8. | -4. | 27. | SCHEDULED | NECROPSY DAY 20 |
| 29663 G | 12. | 13. | 73. | 1. | 25. | 41. | 67. | 168. | SCHEDULED | NECROPSY DAY 20 |
| 29666 G | 4. | 16. | 50. | 11. | 12. | 20. | 43. | 127. | SCHEDULED | NECROPSY DAY 20 |
| 29667 G | 5. | 10. | 55. | 9. | 19. | 24. | 52. | 131. | SCHEDULED | NECROPSY DAY 20 |
| 29668 G | 4. | 6. | 72. | 1. | 37. | 28. | 66. | 155. | SCHEDULED | NECROPSY DAY 20 |
| 29673 G | 9. | 17. | 69. | 5. | 24. | 38. | 67. | 179. | SCHEDULED | NECROPSY DAY 20 |
| 29675 G | -9. | 16. | 61. | 5. | 15. | 17. | 37. | 129. | SCHEDULED | NECROPSY DAY 20 |
| 29685 G | 6. | 7. | 67. | 7. | 15. | 37. | 59. | 147. | SCHEDULED | NECROPSY DAY 20 |
| 29698 G | 3. | 5. | 53. | 5. | 17. | 14. | 36. | 115. | SCHEDULED | NECROPSY DAY 20 |
| 29710 G | 10. | -8. | 66. | 12. | 15. | 16. | 43. | 138. | SCHEDULED | NECROPSY DAY 20 |
| MEAN | 7. | 8. | 63. | 6. | 17. | 26. | 49. | 138. | | |
| S.D. | 6.0 | 6.5 | 10.9 | 5.7 | 6.8 | 7.9 | 11.7 | 18.6 | | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 20
 PROJECT NO.: WIL-15218 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSIOOL
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAMS FROM GROUP 3: 300 MG/KG/DAY | | | | | | | | | | | | |
|------------------|----------------------------------|------|-----|-----|------|-------|-------|-------|-------|-----|------|-----|-----|
| | DAY 0-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | | | | |
| 29592 G | 11. | -3. | 0. | 5. | 8. | 7. | 0. | 5. | 8. | 7. | 0. | 2. | 17. |
| 29596 G | 43. | 4. | 2. | 6. | 9. | 9. | 12. | 6. | 9. | 9. | 12. | 3. | 0. |
| 29607 G | 44. | -1. | 1. | 6. | 0. | 12. | 10. | 5. | 0. | 12. | 10. | 9. | 2. |
| 29611 G | 31. | -6. | 5. | 5. | 2. | 8. | -2. | 8. | 2. | 8. | -2. | 5. | 5. |
| 29612 G | 23. | -5. | 10. | -1. | 6. | 1. | -5. | -1. | 6. | 1. | -5. | 5. | 9. |
| 29614 G | 47. | -1. | 0. | 8. | 9. | 5. | 3. | 8. | 9. | 5. | 3. | 4. | -1. |
| 29620 G | 27. | 8. | 4. | -4. | 2. | 16. | 15. | -4. | 2. | 16. | 15. | -2. | 6. |
| 29622 G | 47. | 5. | -4. | 7. | 2. | 1. | 10. | 7. | -1. | 1. | 10. | 10. | 4. |
| 29625 G | 15. | 0. | 0. | 8. | 6. | 1. | 7. | 8. | 6. | 1. | 7. | 9. | 2. |
| 29629 G | 27. | 2. | 1. | 12. | 4. | -2. | 15. | 12. | 4. | -2. | 15. | 1. | 8. |
| 29631 G | 30. | -3. | 4. | 8. | 5. | 1. | -1. | 8. | 5. | 1. | -1. | 15. | 1. |
| 29636 G | 27. | -1. | 1. | 9. | 2. | 5. | 13. | 9. | 2. | 5. | 13. | 3. | 2. |
| 29637 G | 6. | -8. | -3. | 6. | 14. | 20. | -10. | 6. | 14. | 20. | -10. | 10. | 16. |
| 29648 G | 26. | 1. | 1. | 3. | 7. | 1. | 9. | 3. | 7. | 1. | 9. | 3. | 0. |
| 29649 G | 34. | 2. | 2. | 5. | 6. | 7. | 4. | 5. | 6. | 7. | 4. | 2. | 6. |
| 29650 G | 21. | -13. | -1. | 5. | 14. | 2. | -1. | 5. | 14. | 2. | -1. | 7. | 17. |
| 29657 G | 30. | -9. | 3. | 2. | 3. | 6. | 5. | 2. | 3. | 6. | 5. | 15. | 1. |
| 29664 G | 16. | -6. | 0. | 3. | 8. | 9. | 3. | 3. | 8. | 9. | 3. | 6. | 4. |
| 29670 G | 28. | -8. | 12. | -1. | 1. | -3. | 20. | -1. | 1. | -3. | 20. | 14. | 1. |
| 29672 NG | 40. | 1. | -2. | 5. | -1. | 7. | 3. | 5. | -1. | 7. | 3. | -5. | 3. |
| 29676 G | 27. | 3. | -1. | 2. | 7. | 13. | 0. | 2. | 7. | 13. | 0. | 9. | 6. |
| 29677 G | 32. | -2. | 1. | 6. | 10. | 3. | 4. | 3. | 10. | 3. | 4. | 5. | 2. |
| 29678 G | 19. | 0. | 3. | 2. | 2. | 8. | 2. | 2. | 2. | 8. | 2. | 7. | 10. |
| 29688 G | 24. | 11. | -2. | 6. | 7. | 6. | 4. | 6. | 7. | 6. | 4. | 7. | 3. |
| 29700 G | 27. | -1. | -6. | 9. | 12. | 0. | 2. | 9. | 12. | 0. | 2. | -2. | 11. |
| MEAN | 28. | -1. | 1. | 5. | 6. | 6. | 5. | 6. | 6. | 6. | 5. | 6. | 6. |
| S.D. | 10.5 | 5.5 | 3.9 | 3.6 | 4.2 | 5.7 | 7.0 | 4.7 | 4.7 | 5.7 | 7.0 | 4.7 | 5.4 |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 20
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAMS FROM GROUP 3: 300 MG/KG/DAY | | | | | | | | | |
|---------------------|----------------------------------|-------|-------|-----|------|-------|------|------|-----------|-----------------|
| | DAY14-15 | 15-16 | 16-20 | 6-9 | 9-12 | 12-16 | 6-16 | 0-20 | | |
| 29592 G | 12. | 10. | 69. | 2. | 15. | 41. | 58. | 138. | SCHEDULED | NECROPSY DAY 20 |
| 29596 G | 10. | 17. | 60. | 12. | 30. | 30. | 72. | 175. | SCHEDULED | NECROPSY DAY 20 |
| 29607 G | 10. | 13. | 69. | 6. | 22. | 34. | 62. | 175. | SCHEDULED | NECROPSY DAY 20 |
| 29611 G | 1. | 8. | 25. | 4. | 8. | 19. | 31. | 87. | SCHEDULED | NECROPSY DAY 20 |
| 29612 G | 1. | 6. | 22. | 4. | 2. | 21. | 27. | 72. | SCHEDULED | NECROPSY DAY 20 |
| 29614 G | 17. | 9. | 64. | 7. | 17. | 29. | 53. | 164. | SCHEDULED | NECROPSY DAY 20 |
| 29620 G | 12. | 16. | 44. | 8. | 33. | 32. | 73. | 144. | SCHEDULED | NECROPSY DAY 20 |
| 29622 G | 5. | 10. | 66. | 8. | 10. | 29. | 47. | 160. | SCHEDULED | NECROPSY DAY 20 |
| 29625 G | 14. | 8. | 65. | 8. | 14. | 33. | 55. | 135. | SCHEDULED | NECROPSY DAY 20 |
| 29629 G | 8. | 5. | 50. | 15. | 17. | 22. | 54. | 131. | SCHEDULED | NECROPSY DAY 20 |
| 29631 G | 10. | 12. | 68. | 9. | 5. | 38. | 52. | 150. | SCHEDULED | NECROPSY DAY 20 |
| 29636 G | 11. | 4. | 53. | 9. | 20. | 20. | 49. | 129. | SCHEDULED | NECROPSY DAY 20 |
| 29637 G | 16. | 16. | 82. | -5. | 24. | 58. | 77. | 165. | SCHEDULED | NECROPSY DAY 20 |
| 29648 G | 7. | 2. | 43. | 5. | 17. | 12. | 34. | 103. | SCHEDULED | NECROPSY DAY 20 |
| 29649 G | 5. | 11. | 78. | 9. | 17. | 24. | 50. | 162. | SCHEDULED | NECROPSY DAY 20 |
| 29650 G | 5. | 11. | 64. | -9. | 15. | 40. | 46. | 131. | SCHEDULED | NECROPSY DAY 20 |
| 29657 G | 11. | 6. | 69. | -4. | 14. | 33. | 43. | 142. | SCHEDULED | NECROPSY DAY 20 |
| 29664 G | 11. | 14. | 63. | -3. | 20. | 35. | 52. | 131. | SCHEDULED | NECROPSY DAY 20 |
| 29670 G | 14. | 7. | 72. | 3. | 18. | 36. | 57. | 157. | SCHEDULED | NECROPSY DAY 20 |
| 29672 NG | -6. | -7. | -1. | 4. | 9. | -15. | -2. | 37. | SCHEDULED | NECROPSY DAY 20 |
| 29676 G | 12. | 14. | 71. | 4. | 20. | 41. | 65. | 163. | SCHEDULED | NECROPSY DAY 20 |
| 29677 G | 12. | 12. | 60. | 5. | 17. | 31. | 53. | 145. | SCHEDULED | NECROPSY DAY 20 |
| 29678 G | 11. | 8. | 54. | 5. | 12. | 36. | 53. | 126. | SCHEDULED | NECROPSY DAY 20 |
| 29688 G | 7. | 15. | 66. | 15. | 17. | 32. | 64. | 154. | SCHEDULED | NECROPSY DAY 20 |
| 29700 G | 11. | 11. | 62. | 2. | 14. | 31. | 47. | 136. | SCHEDULED | NECROPSY DAY 20 |
| MEAN | 10. | 10. | 60. | 5. | 17. | 32. | 53. | 141. | | |
| S.D. | 4.1 | 4.0 | 14.6 | 5.9 | 6.9 | 9.3 | 12.3 | 25.6 | | |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 20
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

| PREGNANCY STATUS | DAMS FROM GROUP 4: 1000 MG/KG/DAY | | | | | | | | | | | | | |
|------------------|-----------------------------------|------|------|------|------|-------|-------|-------|-------|--|--|--|--|--|
| | DAY 0-6 | 6-7 | 7-8 | 8-9 | 9-10 | 10-11 | 11-12 | 12-13 | 13-14 | | | | | |
| 29597 G | 16. | 0. | -23. | 17. | 13. | 12. | 8. | 3. | -1. | | | | | |
| 29598 G | 34. | -6. | 5. | 3. | 6. | -2. | 7. | 8. | 8. | | | | | |
| 29608 G | 29. | -1. | 3. | 8. | -2. | 4. | 9. | 11. | 1. | | | | | |
| 29613 G | 28. | -7. | 0. | 4. | 8. | 1. | 5. | 8. | 1. | | | | | |
| 29616 G | 32. | -14. | 4. | 7. | 5. | 7. | 2. | 7. | 5. | | | | | |
| 29618 G | 29. | 1. | -5. | -1. | 2. | 9. | 9. | 3. | 6. | | | | | |
| 29621 G | 22. | -15. | 22. | 1. | 6. | 7. | 8. | 7. | 1. | | | | | |
| 29626 G | 41. | -5. | 4. | 3. | 2. | 7. | 8. | 6. | 3. | | | | | |
| 29632 G | 36. | -4. | 5. | -13. | 1. | 11. | 9. | 13. | 2. | | | | | |
| 29638 G | 42. | -1. | -2. | 3. | 6. | -1. | 6. | 6. | 2. | | | | | |
| 29641 G | 14. | -3. | -3. | 3. | 7. | 20. | -5. | 5. | 4. | | | | | |
| 29643 G | 32. | -5. | -8. | 13. | 1. | -2. | 9. | 8. | 8. | | | | | |
| 29651 G | 30. | -10. | 0. | 8. | 14. | 0. | 17. | 3. | 3. | | | | | |
| 29654 NG | 34. | 3. | -2. | 4. | 11. | -4. | -2. | -7. | 8. | | | | | |
| 29655 G | 45. | -9. | 8. | 2. | -2. | 12. | 2. | 12. | 14. | | | | | |
| 29658 NG | 7. | -3. | 4. | -1. | 3. | -10. | 1. | 4. | 5. | | | | | |
| 29659 G | 26. | -15. | -5. | 9. | 4. | 2. | -3. | 9. | 8. | | | | | |
| 29665 G | 36. | -7. | -2. | 6. | 2. | 17. | 6. | 3. | 1. | | | | | |
| 29671 G | 46. | -2. | -3. | -2. | 8. | 5. | -1. | 10. | 3. | | | | | |
| 29679 G | 26. | 4. | 3. | -5. | 4. | 10. | 7. | -1. | 5. | | | | | |
| 29680 G | 29. | -18. | 1. | 17. | -6. | 10. | 2. | 5. | 1. | | | | | |
| 29681 NG | 33. | -4. | -9. | 5. | -1. | 1. | 2. | -12. | 10. | | | | | |
| 29682 G | 42. | -14. | -17. | 22. | 10. | 12. | 9. | 7. | 7. | | | | | |
| 29694 G | 31. | -14. | 10. | 3. | 5. | 7. | 2. | 7. | -2. | | | | | |
| 29704 G | 32. | -3. | 0. | 4. | 10. | 6. | 5. | -1. | 9. | | | | | |
| MEAN | 32. | -7. | 0. | 5. | 5. | 7. | 6. | 6. | 4. | | | | | |
| S.D. | 8.4 | 6.1 | 9.0 | 7.7 | 4.9 | 5.9 | 4.8 | 3.7 | 3.8 | | | | | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | | | | | |

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G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 20
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

| PREGNANCY STATUS | | DAY14-15 | 15-16 | 16-20 | 6-9 | 9-12 | 12-16 | 6-16 | 0-20 |
|-----------------------------------|----|----------|-------|-------|------|------|-------|------|--------------------------------|
| DAMS FROM GROUP 4: 1000 MG/KG/DAY | | | | | | | | | |
| 29597 | G | 2. | 12. | 48. | -6. | 33. | 16. | 43. | 107. SCHEDULED NECROPSY DAY 20 |
| 29598 | G | 1. | 13. | 55. | 2. | 11. | 30. | 43. | 132. SCHEDULED NECROPSY DAY 20 |
| 29608 | G | 12. | 8. | 63. | 10. | 11. | 32. | 53. | 145. SCHEDULED NECROPSY DAY 20 |
| 29613 | G | 5. | 10. | 55. | -3. | 14. | 24. | 35. | 118. SCHEDULED NECROPSY DAY 20 |
| 29616 | G | 12. | 8. | 64. | -3. | 14. | 32. | 43. | 139. SCHEDULED NECROPSY DAY 20 |
| 29618 | G | 4. | 12. | 48. | -5. | 20. | 25. | 40. | 117. SCHEDULED NECROPSY DAY 20 |
| 29621 | G | 9. | 13. | 70. | 8. | 21. | 30. | 59. | 151. SCHEDULED NECROPSY DAY 20 |
| 29626 | G | 7. | 6. | 55. | 2. | 17. | 22. | 41. | 137. SCHEDULED NECROPSY DAY 20 |
| 29632 | G | 9. | 8. | 54. | -12. | 21. | 32. | 41. | 131. SCHEDULED NECROPSY DAY 20 |
| 29638 | G | 6. | 15. | 62. | 0. | 11. | 29. | 40. | 144. SCHEDULED NECROPSY DAY 20 |
| 29641 | G | 15. | 14. | 62. | -3. | 22. | 38. | 57. | 133. SCHEDULED NECROPSY DAY 20 |
| 29643 | G | 3. | 20. | 77. | 0. | 8. | 39. | 47. | 156. SCHEDULED NECROPSY DAY 20 |
| 29651 | G | 8. | 15. | 78. | -2. | 31. | 29. | 58. | 166. SCHEDULED NECROPSY DAY 20 |
| 29654 | NG | 2. | -6. | 5. | 5. | 5. | -3. | 7. | 46. SCHEDULED NECROPSY DAY 20 |
| 29655 | G | 4. | 6. | 56. | 1. | 12. | 36. | 49. | 150. SCHEDULED NECROPSY DAY 20 |
| 29658 | NG | -2. | -1. | 7. | 0. | -6. | 6. | 0. | 14. SCHEDULED NECROPSY DAY 20 |
| 29659 | G | 3. | 4. | 27. | -11. | 3. | 24. | 16. | 69. SCHEDULED NECROPSY DAY 20 |
| 29665 | G | 14. | 14. | 45. | -3. | 25. | 32. | 54. | 135. SCHEDULED NECROPSY DAY 20 |
| 29671 | G | 8. | 5. | 59. | -7. | 12. | 26. | 31. | 136. SCHEDULED NECROPSY DAY 20 |
| 29679 | G | 9. | 12. | 61. | 2. | 21. | 25. | 48. | 135. SCHEDULED NECROPSY DAY 20 |
| 29680 | G | 4. | 5. | 64. | 0. | 6. | 15. | 21. | 114. SCHEDULED NECROPSY DAY 20 |
| 29681 | NG | 8. | -5. | 1. | -8. | 2. | 1. | -5. | 29. SCHEDULED NECROPSY DAY 20 |
| 29682 | G | 9. | 13. | 69. | -9. | 31. | 36. | 58. | 169. SCHEDULED NECROPSY DAY 20 |
| 29694 | G | 12. | 9. | 73. | -1. | 14. | 26. | 39. | 143. SCHEDULED NECROPSY DAY 20 |
| 29704 | G | 13. | 12. | 63. | 1. | 21. | 33. | 55. | 150. SCHEDULED NECROPSY DAY 20 |
| MEAN | | 8. | 11. | 59. | -2. | 17. | 29. | 44. | 135. |
| S.D. | | 4.1 | 4.1 | 11.4 | 5.4 | 8.1 | 6.3 | 11.5 | 21.5 |
| N | | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 21
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL GRAVID UTERINE WT. AND NET BODY WT. CHANGE (GRAMS)

| DAM # | PREGNANCY STATUS | INITIAL BODY WT. | TERMINAL BODY WT. | GRAVID UTERINE WT. | NET BODY WT. | NET BODY WT. CHANGE |
|-------|------------------|----------------------|-------------------|--------------------|--------------|---------------------|
| | | GROUP 1: 0 MG/KG/DAY | | | | |
| 29593 | NG | 261. | 305. | NA | NA | NA |
| 29599 | G | 255. | 384. | 75.5 | 308.5 | 53.5 |
| 29601 | G | 261. | 449. | 103.7 | 345.3 | 84.3 |
| 29602 | G | 250. | 391. | 85.5 | 305.5 | 55.5 |
| 29609 | G | 244. | 315. | 7.9 | 307.1 | 63.1 |
| 29615 | G | 246. | 379. | 74.5 | 304.5 | 58.5 |
| 29619 | G | 257. | 411. | 77.1 | 333.9 | 76.9 |
| 29623 | G | 255. | 394. | 75.0 | 319.0 | 64.0 |
| 29628 | G | 248. | 409. | 80.5 | 328.5 | 80.5 |
| 29634 | G | 251. | 389. | 85.7 | 303.3 | 52.3 |
| 29639 | G | 248. | 385. | 72.7 | 312.3 | 64.3 |
| 29640 | G | 253. | 368. | 55.4 | 312.6 | 59.6 |
| 29644 | G | 272. | 394. | 57.1 | 336.9 | 64.9 |
| 29647 | G | 258. | 409. | 68.0 | 341.0 | 83.0 |
| 29652 | G | 239. | 325. | 7.3 | 317.7 | 78.7 |
| 29660 | G | 246. | 381. | 79.1 | 301.9 | 55.9 |
| 29661 | G | 231. | 367. | 73.8 | 293.2 | 62.2 |
| 29662 | G | 245. | 376. | 74.1 | 301.9 | 56.9 |
| 29669 | G | 236. | 383. | 75.0 | 308.0 | 72.0 |
| 29674 | G | 250. | 374. | 76.8 | 297.2 | 47.2 |
| 29683 | G | 266. | 381. | 71.3 | 309.7 | 43.7 |
| 29684 | G | 244. | 370. | 65.2 | 304.8 | 60.8 |
| 29695 | G | 240. | 370. | 77.6 | 292.4 | 52.4 |
| 29696 | G | 243. | 385. | 80.6 | 304.4 | 61.4 |
| 29709 | G | 248. | 359. | 61.5 | 297.5 | 49.5 |
| MEAN | | 249. | 381. | 69.2 | 312.0 | 62.5 |
| S.D. | | 9.3 | 26.6 | 21.34 | 14.91 | 11.40 |
| N | | 24 | 24 | 24 | 24 | 24 |

G = GRAVID, NG = NONGRAVID, NOT INCLUDED IN CALCULATION OF THE MEAN
 NA = NOT APPLICABLE

| DAM # | PREGNANCY STATUS | INITIAL BODY WT. | TERMINAL BODY WT. | GRAVID UTERINE WT. | NET BODY WT. | NET BODY WT. CHANGE |
|-----------------------|------------------|------------------|-------------------|--------------------|--------------|---------------------|
| GROUP 2: 30 MG/KG/DAY | | | | | | |
| 29591 | G | 253. | 400. | 76.7 | 323.3 | 70.3 |
| 29595 | G | 250. | 391. | 90.9 | 300.1 | 50.1 |
| 29600 | G | 257. | 388. | 88.3 | 299.7 | 42.7 |
| 29603 | NG | 252. | 273. | NA | NA | NA |
| 29605 | G | 247. | 363. | 52.9 | 310.1 | 63.1 |
| 29606 | G | 271. | 427. | 92.1 | 334.9 | 63.9 |
| 29610 | G | 256. | 388. | 77.7 | 310.3 | 54.3 |
| 29617 | G | 227. | 331. | 54.7 | 276.3 | 49.3 |
| 29624 | G | 252. | 396. | 82.4 | 313.6 | 61.6 |
| 29630 | G | 252. | 391. | 81.2 | 309.8 | 57.8 |
| 29633 | G | 261. | 381. | 78.5 | 302.5 | 41.5 |
| 29635 | G | 249. | 378. | 82.4 | 295.6 | 46.6 |
| 29642 | G | 245. | 370. | 65.9 | 304.1 | 59.1 |
| 29645 | NG | 244. | 256. | NA | NA | NA |
| 29646 | G | 278. | 444. | 112.7 | 331.3 | 53.3 |
| 29653 | NG | 251. | 278. | NA | NA | NA |
| 29663 | G | 279. | 447. | 93.4 | 353.6 | 74.6 |
| 29666 | G | 258. | 385. | 63.2 | 321.8 | 63.8 |
| 29667 | G | 249. | 380. | 73.2 | 306.8 | 57.8 |
| 29668 | G | 256. | 411. | 96.5 | 314.5 | 58.5 |
| 29673 | G | 245. | 424. | 90.4 | 333.6 | 88.6 |
| 29675 | G | 247. | 376. | 74.3 | 301.7 | 54.7 |
| 29685 | G | 246. | 393. | 85.2 | 307.8 | 61.8 |
| 29698 | G | 248. | 363. | 73.1 | 289.9 | 41.9 |
| 29710 | G | 239. | 377. | 72.7 | 304.3 | 65.3 |
| MEAN | | 253. | 391. | 79.9 | 311.2 | 58.2 |
| S.D. | | 11.8 | 27.0 | 13.90 | 16.92 | 11.17 |
| N | | 22 | 22 | 22 | 22 | 22 |

G = GRAVID, NG = NONGRAVID, NOT INCLUDED IN CALCULATION OF THE MEAN
NA = NOT APPLICABLE

| DAM # | PREGNANCY STATUS | INITIAL BODY WT. | TERMINAL BODY WT. | GRAVID UTERINE WT. | NET BODY WT. | NET BODY WT. CHANGE |
|------------------------|------------------|------------------|-------------------|--------------------|--------------|---------------------|
| GROUP 3: 300 MG/KG/DAY | | | | | | |
| 29592 | G | 275. | 413. | 88.4 | 324.6 | 49.6 |
| 29596 | G | 269. | 444. | 76.0 | 368.0 | 99.0 |
| 29607 | G | 233. | 408. | 94.9 | 313.1 | 80.1 |
| 29611 | G | 237. | 324. | 20.2 | 303.8 | 66.8 |
| 29612 | G | 252. | 324. | 23.5 | 300.5 | 48.5 |
| 29614 | G | 256. | 420. | 84.6 | 335.4 | 79.4 |
| 29620 | G | 254. | 398. | 72.9 | 325.1 | 71.1 |
| 29622 | G | 244. | 404. | 63.4 | 340.6 | 96.6 |
| 29625 | G | 275. | 410. | 85.7 | 324.3 | 49.3 |
| 29629 | G | 258. | 389. | 70.3 | 318.7 | 60.7 |
| 29631 | G | 239. | 389. | 84.1 | 304.9 | 65.9 |
| 29636 | G | 249. | 378. | 68.1 | 309.9 | 60.9 |
| 29637 | G | 273. | 438. | 108.4 | 329.6 | 56.6 |
| 29648 | G | 274. | 377. | 42.8 | 334.2 | 60.2 |
| 29649 | G | 254. | 416. | 90.9 | 325.1 | 71.1 |
| 29650 | G | 250. | 381. | 81.6 | 299.4 | 49.4 |
| 29657 | G | 243. | 385. | 73.2 | 311.8 | 68.8 |
| 29664 | G | 264. | 395. | 82.6 | 312.4 | 48.4 |
| 29670 | G | 250. | 407. | 84.3 | 322.7 | 72.7 |
| 29672 | NG | 239. | 276. | NA | NA | NA |
| 29676 | G | 254. | 417. | 98.8 | 318.2 | 64.2 |
| 29677 | G | 277. | 422. | 83.7 | 338.3 | 61.3 |
| 29678 | G | 261. | 387. | 91.1 | 295.9 | 34.9 |
| 29688 | G | 243. | 397. | 74.9 | 322.1 | 79.1 |
| 29700 | G | 255. | 391. | 91.5 | 299.5 | 44.5 |
| MEAN | | 256. | 396. | 76.5 | 319.9 | 64.1 |
| S.D. | | 12.9 | 28.4 | 21.31 | 16.51 | 15.70 |
| N | | 24 | 24 | 24 | 24 | 24 |

G = GRAVID, NG = NONGRAVID, NOT INCLUDED IN CALCULATION OF THE MEAN
 NA = NOT APPLICABLE

| DAM # | PREGNANCY STATUS | INITIAL BODY WT. | TERMINAL BODY WT. | GRAVID UTERINE WT. | NET BODY WT. | NET BODY WT. CHANGE |
|-------------------------|------------------|------------------|-------------------|--------------------|--------------|---------------------|
| GROUP 4: 1000 MG/KG/DAY | | | | | | |
| 29597 | G | 234. | 341. | 47.5 | 293.5 | 59.5 |
| 29598 | G | 263. | 395. | 73.2 | 321.8 | 58.8 |
| 29608 | G | 246. | 391. | 76.9 | 314.1 | 68.1 |
| 29613 | G | 233. | 351. | 75.7 | 275.3 | 42.3 |
| 29616 | G | 252. | 391. | 82.3 | 308.7 | 56.7 |
| 29618 | G | 264. | 381. | 70.8 | 310.2 | 46.2 |
| 29621 | G | 250. | 401. | 88.4 | 312.6 | 62.6 |
| 29626 | G | 247. | 384. | 63.2 | 320.8 | 73.8 |
| 29632 | G | 240. | 371. | 65.8 | 305.2 | 65.2 |
| 29638 | G | 250. | 394. | 85.3 | 308.7 | 58.7 |
| 29641 | G | 257. | 390. | 74.3 | 315.7 | 58.7 |
| 29643 | G | 278. | 434. | 93.8 | 340.2 | 62.2 |
| 29651 | G | 252. | 418. | 96.4 | 321.6 | 69.6 |
| 29654 | NG | 249. | 295. | NA | NA | NA |
| 29655 | G | 267. | 417. | 62.1 | 354.9 | 87.9 |
| 29658 | NG | 243. | 257. | NA | NA | NA |
| 29659 | G | 258. | 327. | 14.5 | 312.5 | 54.5 |
| 29665 | G | 238. | 373. | 69.4 | 303.6 | 65.6 |
| 29671 | G | 220. | 356. | 73.0 | 283.0 | 63.0 |
| 29679 | G | 265. | 400. | 84.0 | 316.0 | 51.0 |
| 29680 | G | 271. | 385. | 88.7 | 296.3 | 25.3 |
| 29681 | NG | 271. | 300. | NA | NA | NA |
| 29682 | G | 229. | 398. | 68.2 | 329.8 | 100.8 |
| 29694 | G | 260. | 403. | 82.6 | 320.4 | 60.4 |
| 29704 | G | 251. | 401. | 84.8 | 316.2 | 65.2 |
| MEAN | | 251. | 386. | 73.7 | 312.8 | 61.6 |
| S.D. | | 14.6 | 25.5 | 17.52 | 17.25 | 14.92 |
| N | | 22 | 22 | 22 | 22 | 22 |

G = GRAVID, NG = NONGRAVID, NOT INCLUDED IN CALCULATION OF THE MEAN
 NA = NOT APPLICABLE

TABLE 22
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/ANIMAL/DAY)

| PREGNANCY STATUS | PREGNANCY STATUS | | | | | | | |
|--------------------------------|------------------|-----|------|-------|-------|------|------|---------------------------|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 | |
| DAMS FROM GROUP 1: 0 MG/KG/DAY | | | | | | | | |
| 29593 NG | 24. | 21. | 20. | 18. | 22. | 20. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29599 G | 22. | 19. | 17. | 23. | 30. | 20. | 22. | SCHEDULED NECROPSY DAY 20 |
| 29601 G | 27. | 22. | 24. | 23. | 28. | 23. | 25. | SCHEDULED NECROPSY DAY 20 |
| 29602 G | 25. | 22. | 21. | 21. | 29. | 21. | 24. | SCHEDULED NECROPSY DAY 20 |
| 29609 G | 22. | 17. | 19. | 19. | 25. | 19. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29615 G | 19. | 17. | 19. | 21. | 27. | 19. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29619 G | 24. | 19. | 21. | 21. | 30. | 21. | 24. | SCHEDULED NECROPSY DAY 20 |
| 29623 G | 21. | 15. | 19. | 19. | 28. | 18. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29628 G | 24. | 20. | 24. | 26. | 30. | 24. | 25. | SCHEDULED NECROPSY DAY 20 |
| 29634 G | 20. | 19. | 21. | 20. | 28. | 20. | 22. | SCHEDULED NECROPSY DAY 20 |
| 29639 G | 21. | 18. | 18. | 19. | 27. | 19. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29640 G | 23. | 19. | 20. | 20. | 28. | 20. | 22. | SCHEDULED NECROPSY DAY 20 |
| 29644 G | 28. | 21. | 15. | 33. | 38. | 24. | 28. | SCHEDULED NECROPSY DAY 20 |
| 29647 G | 24. | 21. | 21. | 23. | 31. | 22. | 24. | SCHEDULED NECROPSY DAY 20 |
| 29652 G | 22. | 19. | 21. | 20. | 24. | 20. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29660 G | 20. | 17. | 17. | 23. | 30. | 19. | 22. | SCHEDULED NECROPSY DAY 20 |
| 29661 G | 22. | 16. | 19. | 20. | 26. | 19. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29662 G | 19. | 14. | 20. | 21. | 27. | 18. | 20. | SCHEDULED NECROPSY DAY 20 |
| 29669 G | 23. | 14. | 21. | 20. | 26. | 19. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29674 G | 21. | 18. | 20. | 23. | 26. | 20. | 22. | SCHEDULED NECROPSY DAY 20 |
| 29683 G | 19. | 19. | 19. | 21. | 28. | 20. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29684 G | 21. | 15. | 20. | 20. | 25. | 19. | 21. | SCHEDULED NECROPSY DAY 20 |
| 29695 G | 20. | 18. | 16. | 19. | 25. | 18. | 20. | SCHEDULED NECROPSY DAY 20 |
| 29696 G | 23. | 19. | 20. | 22. | 28. | 20. | 23. | SCHEDULED NECROPSY DAY 20 |
| 29709 G | 20. | 15. | 19. | 19. | 24. | 18. | 20. | SCHEDULED NECROPSY DAY 20 |

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| MEAN | 22. | 18. | 20. | 22. | 28. | 20. | 22. |
| S.D. | 2.4 | 2.3 | 2.1 | 3.0 | 2.9 | 1.7 | 1.9 |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 22
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/ANIMAL/DAY)

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| PREGNANCY STATUS | 30 MG/KG/DAY | | | | | | | 0-20 |
|--------------------|--------------|-----|------|-------|-------|------|-------------------------------|------|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 | |
| DAMS FROM GROUP 2: | 30 MG/KG/DAY | | | | | | | |
| 29591 G | 22. | 19. | 20. | 20. | 28. | 20. | 22. SCHEDULED NECROPSY DAY 20 | |
| 29595 G | 21. | 18. | 19. | 19. | 26. | 19. | 21. SCHEDULED NECROPSY DAY 20 | |
| 29600 G | 20. | 13. | 18. | 17. | 28. | 16. | 19. SCHEDULED NECROPSY DAY 20 | |
| 29603 NG | 17. | 15. | 18. | 15. | 19. | 16. | 17. SCHEDULED NECROPSY DAY 20 | |
| 29605 G | 22. | 22. | 23. | 22. | 29. | 22. | 23. SCHEDULED NECROPSY DAY 20 | |
| 29606 G | 24. | 22. | 25. | 24. | 31. | 24. | 25. SCHEDULED NECROPSY DAY 20 | |
| 29610 G | 21. | 17. | 20. | 20. | 26. | 19. | 21. SCHEDULED NECROPSY DAY 20 | |
| 29617 G | 20. | 17. | 17. | 18. | 24. | 17. | 19. SCHEDULED NECROPSY DAY 20 | |
| 29624 G | 20. | 17. | 19. | 21. | 29. | 19. | 21. SCHEDULED NECROPSY DAY 20 | |
| 29630 G | 26. | 20. | 21. | 23. | 27. | 21. | 24. SCHEDULED NECROPSY DAY 20 | |
| 29633 G | 21. | 22. | 21. | 18. | 26. | 20. | 21. SCHEDULED NECROPSY DAY 20 | |
| 29635 G | 13. | 21. | 22. | 22. | 30. | 22. | 21. SCHEDULED NECROPSY DAY 20 | |
| 29642 G | 23. | 20. | 21. | 21. | 25. | 20. | 22. SCHEDULED NECROPSY DAY 20 | |
| 29645 NG | 17. | 16. | 16. | 11. | 14. | 14. | 15. SCHEDULED NECROPSY DAY 20 | |
| 29646 G | 25. | 21. | 20. | 21. | 30. | 21. | 24. SCHEDULED NECROPSY DAY 20 | |
| 29653 NG | 21. | 16. | 15. | 14. | 16. | 15. | 17. SCHEDULED NECROPSY DAY 20 | |
| 29663 G | 25. | 21. | 23. | 25. | 34. | 23. | 26. SCHEDULED NECROPSY DAY 20 | |
| 29666 G | 24. | 20. | 21. | 20. | 29. | 20. | 23. SCHEDULED NECROPSY DAY 20 | |
| 29667 G | 20. | 17. | 19. | 19. | 26. | 19. | 20. SCHEDULED NECROPSY DAY 20 | |
| 29668 G | 19. | 15. | 22. | 23. | 29. | 20. | 22. SCHEDULED NECROPSY DAY 20 | |
| 29673 G | 23. | 20. | 22. | 24. | 32. | 22. | 24. SCHEDULED NECROPSY DAY 20 | |
| 29675 G | 21. | 18. | 20. | 21. | 29. | 20. | 22. SCHEDULED NECROPSY DAY 20 | |
| 29685 G | 20. | 18. | 18. | 23. | 28. | 20. | 22. SCHEDULED NECROPSY DAY 20 | |
| 29698 G | 20. | 17. | 18. | 19. | 23. | 18. | 20. SCHEDULED NECROPSY DAY 20 | |
| 29710 G | 23. | 19. | 20. | 19. | 29. | 19. | 22. SCHEDULED NECROPSY DAY 20 | |
| MEAN | 22. | 19. | 20. | 21. | 28. | 20. | 22. | |
| S.D. | 2.7 | 2.4 | 1.9 | 2.2 | 2.6 | 1.9 | 1.8 | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 22
 PROJECT NO.: WIL-15218
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSIOOL
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/ANIMAL/DAY)

| PREGNANCY STATUS | DAMS FROM GROUP 3: 300 MG/KG/DAY | | | | | | |
|------------------|----------------------------------|-----|------|-------|-------|------|-------------------------------|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 |
| 29592 G | 18. | 18. | 19. | 23. | 29. | 20. | 21. SCHEDULED NECROPSY DAY 20 |
| 29596 G | 29. | 25. | 29. | 27. | 33. | 27. | 28. SCHEDULED NECROPSY DAY 20 |
| 29607 G | 22. | 17. | 21. | 22. | 29. | 20. | 23. SCHEDULED NECROPSY DAY 20 |
| 29611 G | 23. | 18. | 21. | 20. | 26. | 20. | 22. SCHEDULED NECROPSY DAY 20 |
| 29612 G | 23. | 17. | 16. | 18. | 25. | 17. | 20. SCHEDULED NECROPSY DAY 20 |
| 29614 G | 25. | 22. | 21. | 20. | 29. | 21. | 24. SCHEDULED NECROPSY DAY 20 |
| 29620 G | 22. | 19. | 20. | 24. | 29. | 21. | 23. SCHEDULED NECROPSY DAY 20 |
| 29622 G | 25. | 21. | 20. | 22. | 31. | 21. | 24. SCHEDULED NECROPSY DAY 20 |
| 29625 G | 21. | 19. | 19. | 23. | 31. | 21. | 23. SCHEDULED NECROPSY DAY 20 |
| 29629 G | 21. | 17. | 19. | 20. | 26. | 19. | 21. SCHEDULED NECROPSY DAY 20 |
| 29631 G | 21. | 18. | 20. | 22. | 28. | 20. | 22. SCHEDULED NECROPSY DAY 20 |
| 29636 G | 21. | 19. | 22. | 22. | 29. | 21. | 23. SCHEDULED NECROPSY DAY 20 |
| 29637 G | 17. | 14. | 22. | 27. | 34. | 21. | 22. SCHEDULED NECROPSY DAY 20 |
| 29648 G | 24. | 22. | 23. | 20. | 27. | 21. | 23. SCHEDULED NECROPSY DAY 20 |
| 29649 G | 23. | 21. | 22. | 21. | 32. | 21. | 24. SCHEDULED NECROPSY DAY 20 |
| 29650 G | 21. | 11. | 19. | 21. | 28. | 17. | 20. SCHEDULED NECROPSY DAY 20 |
| 29657 G | 20. | 13. | 18. | 21. | 29. | 18. | 21. SCHEDULED NECROPSY DAY 20 |
| 29664 G | 19. | 16. | 19. | 22. | 28. | 19. | 21. SCHEDULED NECROPSY DAY 20 |
| 29670 G | 22. | 14. | 17. | 24. | 32. | 19. | 23. SCHEDULED NECROPSY DAY 20 |
| 29672 NG | 23. | 21. | 21. | 14. | 19. | 19. | 20. SCHEDULED NECROPSY DAY 20 |
| 29676 G | 22. | 18. | 19. | 21. | 30. | 20. | 22. SCHEDULED NECROPSY DAY 20 |
| 29677 G | 24. | 21. | 22. | 22. | 27. | 21. | 23. SCHEDULED NECROPSY DAY 20 |
| 29678 G | 22. | 19. | 21. | 24. | 27. | 21. | 23. SCHEDULED NECROPSY DAY 20 |
| 29688 G | 23. | 26. | 23. | 25. | 31. | 24. | 25. SCHEDULED NECROPSY DAY 20 |
| 29700 G | 20. | 18. | 19. | 20. | 26. | 19. | 21. SCHEDULED NECROPSY DAY 20 |
| MEAN | 22. | 18. | 20. | 22. | 29. | 20. | 23. |
| S.D. | 2.5 | 3.5 | 2.6 | 2.2 | 2.4 | 2.1 | 1.7 |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 22
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/ANIMAL/DAY)

| PREGNANCY STATUS | DAMS FROM GROUP 4: 1000 MG/KG/DAY | | | | | | | | | | |
|------------------|-----------------------------------|-----|------|-------|-------|------|------|---------------------------|--|--|--|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 | | | | |
| 29597 G | 18. | 8. | 19. | 20. | 30. | 16. | 19. | SCHEDULED NECROPSY DAY 20 | | | |
| 29598 G | 24. | 21. | 18. | 21. | 29. | 20. | 23. | SCHEDULED NECROPSY DAY 20 | | | |
| 29608 G | 23. | 20. | 20. | 24. | 33. | 21. | 24. | SCHEDULED NECROPSY DAY 20 | | | |
| 29613 G | 20. | 16. | 18. | 18. | 24. | 17. | 19. | SCHEDULED NECROPSY DAY 20 | | | |
| 29616 G | 20. | 17. | 19. | 22. | 29. | 20. | 22. | SCHEDULED NECROPSY DAY 20 | | | |
| 29618 G | 24. | 15. | 16. | 19. | 23. | 17. | 20. | SCHEDULED NECROPSY DAY 20 | | | |
| 29621 G | 19. | 16. | 21. | 23. | 29. | 20. | 21. | SCHEDULED NECROPSY DAY 20 | | | |
| 29626 G | 22. | 16. | 20. | 21. | 29. | 19. | 22. | SCHEDULED NECROPSY DAY 20 | | | |
| 29632 G | 22. | 15. | 18. | 25. | 30. | 20. | 23. | SCHEDULED NECROPSY DAY 20 | | | |
| 29638 G | 26. | 22. | 20. | 22. | 30. | 21. | 24. | SCHEDULED NECROPSY DAY 20 | | | |
| 29641 G | 20. | 15. | 18. | 23. | 31. | 19. | 22. | SCHEDULED NECROPSY DAY 20 | | | |
| 29643 G | 24. | 19. | 17. | 23. | 30. | 20. | 23. | SCHEDULED NECROPSY DAY 20 | | | |
| 29651 G | 25. | 14. | 22. | 22. | 29. | 20. | 23. | SCHEDULED NECROPSY DAY 20 | | | |
| 29654 NG | 24. | 21. | 20. | 17. | 21. | 19. | 21. | SCHEDULED NECROPSY DAY 20 | | | |
| 29655 G | 30. | 26. | 23. | 31. | 35. | 27. | 29. | SCHEDULED NECROPSY DAY 20 | | | |
| 29658 NG | 20. | 17. | 14. | 14. | 20. | 15. | 17. | SCHEDULED NECROPSY DAY 20 | | | |
| 29659 G | 20. | 15. | 15. | 23. | 28. | 18. | 21. | SCHEDULED NECROPSY DAY 20 | | | |
| 29665 G | 22. | 15. | 19. | 21. | 26. | 19. | 21. | SCHEDULED NECROPSY DAY 20 | | | |
| 29671 G | 23. | 16. | 17. | 19. | 27. | 17. | 21. | SCHEDULED NECROPSY DAY 20 | | | |
| 29679 G | 22. | 20. | 21. | 22. | 30. | 21. | 23. | SCHEDULED NECROPSY DAY 20 | | | |
| 29680 G | 23. | 17. | 18. | 20. | 28. | 18. | 21. | SCHEDULED NECROPSY DAY 20 | | | |
| 29681 NG | 24. | 17. | 16. | 18. | 21. | 17. | 20. | SCHEDULED NECROPSY DAY 20 | | | |
| 29682 G | 23. | 9. | 25. | 27. | 34. | 21. | 24. | SCHEDULED NECROPSY DAY 20 | | | |
| 29694 G | 24. | 18. | 19. | 20. | 29. | 19. | 22. | SCHEDULED NECROPSY DAY 20 | | | |
| 29704 G | 23. | 18. | 21. | 23. | 30. | 21. | 23. | SCHEDULED NECROPSY DAY 20 | | | |
| MEAN | 23. | 17. | 19. | 22. | 29. | 20. | 22. | | | | |
| S.D. | 2.6 | 3.9 | 2.3 | 2.9 | 2.8 | 2.2 | 2.1 | | | | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | | | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 23
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/KG/DAY)

| PREGNANCY STATUS | DAMS FROM GROUP 1: 0 MG/KG/DAY | | | | | | | |
|---------------------|--------------------------------|-----|------|-------|-------|------|------|-------------------------------|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 | |
| 29593 | NG | 86. | 70. | 66. | 60. | 73. | 66. | 70. SCHEDULED NECROPSY DAY 20 |
| 29599 | G | 83. | 69. | 60. | 76. | 85. | 69. | 75. SCHEDULED NECROPSY DAY 20 |
| 29601 | G | 93. | 70. | 73. | 64. | 67. | 68. | 74. SCHEDULED NECROPSY DAY 20 |
| 29602 | G | 93. | 76. | 71. | 67. | 81. | 70. | 79. SCHEDULED NECROPSY DAY 20 |
| 29609 | G | 84. | 61. | 67. | 64. | 81. | 66. | 73. SCHEDULED NECROPSY DAY 20 |
| 29615 | G | 73. | 63. | 68. | 70. | 78. | 66. | 72. SCHEDULED NECROPSY DAY 20 |
| 29619 | G | 86. | 63. | 67. | 63. | 79. | 66. | 75. SCHEDULED NECROPSY DAY 20 |
| 29623 | G | 79. | 54. | 65. | 61. | 77. | 60. | 70. SCHEDULED NECROPSY DAY 20 |
| 29628 | G | 90. | 70. | 80. | 79. | 79. | 78. | 80. SCHEDULED NECROPSY DAY 20 |
| 29634 | G | 78. | 69. | 73. | 65. | 79. | 68. | 74. SCHEDULED NECROPSY DAY 20 |
| 29639 | G | 80. | 65. | 62. | 62. | 76. | 65. | 71. SCHEDULED NECROPSY DAY 20 |
| 29640 | G | 86. | 67. | 68. | 65. | 81. | 68. | 74. SCHEDULED NECROPSY DAY 20 |
| 29644 | G | 96. | 68. | 50. | 106. | 104. | 78. | 89. SCHEDULED NECROPSY DAY 20 |
| 29647 | G | 88. | 72. | 70. | 70. | 82. | 71. | 77. SCHEDULED NECROPSY DAY 20 |
| 29652 | G | 86. | 70. | 74. | 67. | 76. | 70. | 74. SCHEDULED NECROPSY DAY 20 |
| 29660 | G | 76. | 62. | 60. | 76. | 85. | 66. | 75. SCHEDULED NECROPSY DAY 20 |
| 29661 | G | 88. | 60. | 69. | 67. | 76. | 67. | 74. SCHEDULED NECROPSY DAY 20 |
| 29662 | G | 75. | 53. | 72. | 70. | 78. | 64. | 70. SCHEDULED NECROPSY DAY 20 |
| 29669 | G | 89. | 51. | 73. | 65. | 73. | 65. | 71. SCHEDULED NECROPSY DAY 20 |
| 29674 | G | 80. | 65. | 68. | 74. | 74. | 68. | 74. SCHEDULED NECROPSY DAY 20 |
| 29683 | G | 71. | 68. | 64. | 67. | 78. | 67. | 69. SCHEDULED NECROPSY DAY 20 |
| 29684 | G | 80. | 54. | 68. | 65. | 72. | 64. | 71. SCHEDULED NECROPSY DAY 20 |
| 29695 | G | 80. | 67. | 58. | 65. | 73. | 65. | 71. SCHEDULED NECROPSY DAY 20 |
| 29696 | G | 90. | 70. | 70. | 72. | 79. | 69. | 78. SCHEDULED NECROPSY DAY 20 |
| 29709 | G | 76. | 55. | 66. | 63. | 71. | 62. | 68. SCHEDULED NECROPSY DAY 20 |
| MEAN | | 83. | 64. | 67. | 69. | 79. | 68. | 74. |
| S.D. | | 6.8 | 6.8 | 6.2 | 9.2 | 6.9 | 4.1 | 4.4 |
| N | | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 23
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/KG/DAY)

| PREGNANCY | | STATUS DAY | | | | | | | | 0-20 | |
|---------------------------------|----|------------|-----|------|-------|-------|------|------|-----------|-----------------|--|
| | | 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 | | | |
| DAMS FROM GROUP 2: 30 MG/KG/DAY | | | | | | | | | | | |
| 29591 | G | 81. | 66. | 65. | 62. | 76. | 65. | 71. | SCHEDULED | NECROPSY DAY 20 | |
| 29595 | G | 80. | 65. | 66. | 62. | 73. | 65. | 71. | SCHEDULED | NECROPSY DAY 20 | |
| 29600 | G | 75. | 48. | 63. | 56. | 80. | 55. | 65. | SCHEDULED | NECROPSY DAY 20 | |
| 29603 | NG | 66. | 58. | 69. | 56. | 70. | 61. | 65. | SCHEDULED | NECROPSY DAY 20 | |
| 29605 | G | 84. | 79. | 79. | 73. | 86. | 76. | 78. | SCHEDULED | NECROPSY DAY 20 | |
| 29606 | G | 83. | 72. | 78. | 69. | 78. | 73. | 76. | SCHEDULED | NECROPSY DAY 20 | |
| 29610 | G | 79. | 61. | 69. | 65. | 73. | 64. | 70. | SCHEDULED | NECROPSY DAY 20 | |
| 29617 | G | 83. | 66. | 64. | 66. | 78. | 64. | 71. | SCHEDULED | NECROPSY DAY 20 | |
| 29624 | G | 77. | 62. | 67. | 69. | 81. | 66. | 71. | SCHEDULED | NECROPSY DAY 20 | |
| 29630 | G | 95. | 69. | 71. | 73. | 75. | 69. | 78. | SCHEDULED | NECROPSY DAY 20 | |
| 29633 | G | 77. | 76. | 71. | 58. | 74. | 67. | 69. | SCHEDULED | NECROPSY DAY 20 | |
| 29635 | G | 52. | 81. | 78. | 72. | 86. | 78. | 73. | SCHEDULED | NECROPSY DAY 20 | |
| 29642 | G | 88. | 71. | 72. | 68. | 72. | 68. | 74. | SCHEDULED | NECROPSY DAY 20 | |
| 29645 | NG | 68. | 61. | 60. | 42. | 54. | 53. | 57. | SCHEDULED | NECROPSY DAY 20 | |
| 29646 | G | 87. | 68. | 63. | 61. | 75. | 65. | 73. | SCHEDULED | NECROPSY DAY 20 | |
| 29653 | NG | 79. | 57. | 54. | 51. | 58. | 54. | 62. | SCHEDULED | NECROPSY DAY 20 | |
| 29663 | G | 85. | 68. | 71. | 71. | 83. | 69. | 77. | SCHEDULED | NECROPSY DAY 20 | |
| 29666 | G | 87. | 67. | 69. | 63. | 81. | 65. | 74. | SCHEDULED | NECROPSY DAY 20 | |
| 29667 | G | 77. | 62. | 65. | 61. | 74. | 64. | 67. | SCHEDULED | NECROPSY DAY 20 | |
| 29668 | G | 72. | 55. | 75. | 70. | 77. | 66. | 72. | SCHEDULED | NECROPSY DAY 20 | |
| 29673 | G | 86. | 69. | 72. | 72. | 82. | 71. | 76. | SCHEDULED | NECROPSY DAY 20 | |
| 29675 | G | 80. | 65. | 69. | 69. | 84. | 68. | 75. | SCHEDULED | NECROPSY DAY 20 | |
| 29685 | G | 78. | 66. | 64. | 74. | 78. | 69. | 74. | SCHEDULED | NECROPSY DAY 20 | |
| 29698 | G | 77. | 62. | 63. | 63. | 68. | 62. | 68. | SCHEDULED | NECROPSY DAY 20 | |
| 29710 | G | 91. | 69. | 69. | 62. | 84. | 65. | 75. | SCHEDULED | NECROPSY DAY 20 | |
| MEAN | | 81. | 67. | 69. | 66. | 78. | 67. | 73. | | | |
| S.D. | | 8.5 | 7.2 | 5.0 | 5.3 | 4.9 | 4.8 | 3.5 | | | |
| N | | 22 | 22 | 22 | 22 | 22 | 22 | 22 | | | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 23
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/KG/DAY)

| PREGNANCY STATUS | DAMS FROM GROUP 3: 300 MG/KG/DAY | | | | | | | |
|---------------------|----------------------------------|------|------|-------|-------|------|------|---------------------------|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 | |
| G | 64. | 63. | 64. | 71. | 77. | 66. | 68. | SCHEDULED NECROPSY DAY 20 |
| G | 100. | 79. | 86. | 74. | 80. | 79. | 81. | SCHEDULED NECROPSY DAY 20 |
| G | 86. | 61. | 72. | 69. | 78. | 67. | 76. | SCHEDULED NECROPSY DAY 20 |
| G | 91. | 67. | 76. | 69. | 83. | 72. | 79. | SCHEDULED NECROPSY DAY 20 |
| G | 87. | 62. | 57. | 62. | 80. | 60. | 70. | SCHEDULED NECROPSY DAY 20 |
| G | 89. | 72. | 66. | 59. | 75. | 65. | 74. | SCHEDULED NECROPSY DAY 20 |
| G | 82. | 66. | 66. | 72. | 77. | 68. | 74. | SCHEDULED NECROPSY DAY 20 |
| G | 93. | 71. | 66. | 68. | 84. | 68. | 77. | SCHEDULED NECROPSY DAY 20 |
| G | 74. | 65. | 62. | 70. | 82. | 68. | 73. | SCHEDULED NECROPSY DAY 20 |
| G | 77. | 59. | 62. | 61. | 71. | 61. | 68. | SCHEDULED NECROPSY DAY 20 |
| G | 83. | 66. | 71. | 73. | 79. | 70. | 76. | SCHEDULED NECROPSY DAY 20 |
| G | 80. | 68. | 75. | 70. | 82. | 71. | 77. | SCHEDULED NECROPSY DAY 20 |
| G | 62. | 51. | 75. | 83. | 86. | 70. | 71. | SCHEDULED NECROPSY DAY 20 |
| G | 84. | 73. | 73. | 61. | 76. | 66. | 73. | SCHEDULED NECROPSY DAY 20 |
| G | 85. | 72. | 72. | 65. | 85. | 68. | 77. | SCHEDULED NECROPSY DAY 20 |
| G | 80. | 42. | 70. | 71. | 80. | 60. | 70. | SCHEDULED NECROPSY DAY 20 |
| G | 78. | 49. | 65. | 70. | 83. | 63. | 73. | SCHEDULED NECROPSY DAY 20 |
| G | 70. | 58. | 66. | 71. | 77. | 64. | 70. | SCHEDULED NECROPSY DAY 20 |
| G | 83. | 50. | 60. | 75. | 86. | 64. | 76. | SCHEDULED NECROPSY DAY 20 |
| NG | 89. | 75. | 73. | 49. | 69. | 67. | 71. | SCHEDULED NECROPSY DAY 20 |
| G | 82. | 64. | 64. | 65. | 79. | 66. | 71. | SCHEDULED NECROPSY DAY 20 |
| G | 82. | 68. | 68. | 64. | 69. | 64. | 69. | SCHEDULED NECROPSY DAY 20 |
| G | 81. | 67. | 72. | 76. | 75. | 70. | 76. | SCHEDULED NECROPSY DAY 20 |
| G | 90. | 94. | 79. | 80. | 85. | 81. | 84. | SCHEDULED NECROPSY DAY 20 |
| G | 74. | 64. | 65. | 65. | 72. | 64. | 70. | SCHEDULED NECROPSY DAY 20 |
| MEAN | 82. | 65. | 69. | 69. | 79. | 67. | 74. | |
| S.D. | 8.7 | 10.6 | 6.6 | 6.0 | 4.7 | 5.1 | 4.2 | |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 23
 PROJECT NO.: WIL-15218 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSFOOL INDIVIDUAL FOOD CONSUMPTION DURING GESTATION (GRAMS/KG/DAY)

| PREGNANCY STATUS | 1000 MG/KG/DAY | | | | | | |
|--------------------|----------------|------|------|-------|-------|------|-------------------------------|
| | DAY 0-6 | 6-9 | 9-12 | 12-16 | 16-20 | 6-16 | 0-20 |
| DAMS FROM GROUP 4: | | | | | | | |
| 29597 G | 74. | 33. | 73. | 71. | 95. | 61. | 71. SCHEDULED NECROPSY DAY 20 |
| 29598 G | 86. | 71. | 59. | 65. | 79. | 65. | 73. SCHEDULED NECROPSY DAY 20 |
| 29608 G | 88. | 72. | 69. | 77. | 92. | 71. | 81. SCHEDULED NECROPSY DAY 20 |
| 29613 G | 81. | 62. | 68. | 64. | 74. | 63. | 69. SCHEDULED NECROPSY DAY 20 |
| 29616 G | 75. | 61. | 66. | 71. | 81. | 68. | 74. SCHEDULED NECROPSY DAY 20 |
| 29618 G | 86. | 52. | 54. | 60. | 64. | 56. | 65. SCHEDULED NECROPSY DAY 20 |
| 29621 G | 73. | 59. | 72. | 73. | 79. | 68. | 70. SCHEDULED NECROPSY DAY 20 |
| 29626 G | 82. | 56. | 67. | 66. | 81. | 63. | 72. SCHEDULED NECROPSY DAY 20 |
| 29632 G | 85. | 55. | 66. | 83. | 87. | 70. | 80. SCHEDULED NECROPSY DAY 20 |
| 29638 G | 96. | 76. | 67. | 70. | 83. | 69. | 78. SCHEDULED NECROPSY DAY 20 |
| 29641 G | 76. | 56. | 64. | 75. | 86. | 66. | 75. SCHEDULED NECROPSY DAY 20 |
| 29643 G | 82. | 62. | 54. | 69. | 76. | 63. | 71. SCHEDULED NECROPSY DAY 20 |
| 29651 G | 94. | 51. | 75. | 69. | 77. | 67. | 75. SCHEDULED NECROPSY DAY 20 |
| 29654 NG | 90. | 74. | 68. | 58. | 72. | 66. | 73. SCHEDULED NECROPSY DAY 20 |
| 29655 G | 103. | 84. | 72. | 90. | 90. | 83. | 88. SCHEDULED NECROPSY DAY 20 |
| 29658 NG | 81. | 68. | 56. | 56. | 79. | 60. | 68. SCHEDULED NECROPSY DAY 20 |
| 29659 G | 74. | 55. | 54. | 79. | 89. | 64. | 74. SCHEDULED NECROPSY DAY 20 |
| 29665 G | 86. | 56. | 67. | 68. | 74. | 66. | 72. SCHEDULED NECROPSY DAY 20 |
| 29671 G | 95. | 61. | 64. | 67. | 83. | 62. | 76. SCHEDULED NECROPSY DAY 20 |
| 29679 G | 79. | 68. | 69. | 68. | 81. | 68. | 74. SCHEDULED NECROPSY DAY 20 |
| 29680 G | 80. | 58. | 60. | 64. | 79. | 59. | 68. SCHEDULED NECROPSY DAY 20 |
| 29681 NG | 83. | 57. | 54. | 61. | 70. | 57. | 68. SCHEDULED NECROPSY DAY 20 |
| 29682 G | 92. | 35. | 90. | 87. | 93. | 74. | 83. SCHEDULED NECROPSY DAY 20 |
| 29694 G | 87. | 63. | 64. | 63. | 79. | 63. | 72. SCHEDULED NECROPSY DAY 20 |
| 29704 G | 86. | 64. | 71. | 73. | 81. | 70. | 75. SCHEDULED NECROPSY DAY 20 |
| MEAN | 85. | 60. | 67. | 71. | 82. | 66. | 74. |
| S.D. | 8.0 | 11.5 | 8.0 | 7.8 | 7.2 | 5.6 | 5.2 |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 |

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

| DAMS FROM GROUP 1: 0 MG/KG/DAY | MATERNAL GROSS OBSERVATION |
|--------------------------------|--|
| 29593 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29599 | NO SIGNIFICANT CHANGES OBSERVED |
| 29601 | NO SIGNIFICANT CHANGES OBSERVED |
| 29602 | HAIR LOSS |
| | LEFT LATERAL ABDOMINAL |
| | ACCESSORY SPLEEN |
| | ONE, 3 X 2 X 1 MM |
| 29609 | NO SIGNIFICANT CHANGES OBSERVED |
| 29615 | NO SIGNIFICANT CHANGES OBSERVED |
| 29619 | NO SIGNIFICANT CHANGES OBSERVED |
| 29623 | NO SIGNIFICANT CHANGES OBSERVED |
| 29628 | NO SIGNIFICANT CHANGES OBSERVED |
| 29634 | NO SIGNIFICANT CHANGES OBSERVED |
| 29639 | NO SIGNIFICANT CHANGES OBSERVED |
| 29640 | NO SIGNIFICANT CHANGES OBSERVED |
| 29644 | NO SIGNIFICANT CHANGES OBSERVED |
| 29647 | NO SIGNIFICANT CHANGES OBSERVED |
| | LUNGS- REDDENED |
| | ALL LOBES |
| 29652 | NO SIGNIFICANT CHANGES OBSERVED |
| 29660 | NO SIGNIFICANT CHANGES OBSERVED |
| 29661 | NO SIGNIFICANT CHANGES OBSERVED |
| 29662 | NO SIGNIFICANT CHANGES OBSERVED |
| 29669 | NO SIGNIFICANT CHANGES OBSERVED |
| 29674 | NO SIGNIFICANT CHANGES OBSERVED |
| 29683 | NO SIGNIFICANT CHANGES OBSERVED |
| 29684 | NO SIGNIFICANT CHANGES OBSERVED |
| 29695 | NO SIGNIFICANT CHANGES OBSERVED |
| 29696 | NO SIGNIFICANT CHANGES OBSERVED |
| 29709 | NO SIGNIFICANT CHANGES OBSERVED |

| DAMS FROM GROUP 2: 30 MG/KG/DAY | MATERNAL GROSS OBSERVATION |
|---------------------------------|--|
| 29591 | NO SIGNIFICANT CHANGES OBSERVED |
| 29595 | NO SIGNIFICANT CHANGES OBSERVED |
| 29600 | NO SIGNIFICANT CHANGES OBSERVED |
| 29603 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29605 | NO SIGNIFICANT CHANGES OBSERVED |
| 29606 | NO SIGNIFICANT CHANGES OBSERVED |
| 29610 | NO SIGNIFICANT CHANGES OBSERVED |
| 29617 | NO SIGNIFICANT CHANGES OBSERVED |
| 29624 | NO SIGNIFICANT CHANGES OBSERVED |
| 29630 | NO SIGNIFICANT CHANGES OBSERVED |
| 29633 | NO SIGNIFICANT CHANGES OBSERVED |
| 29635 | NO SIGNIFICANT CHANGES OBSERVED |
| 29642 | NO SIGNIFICANT CHANGES OBSERVED |
| 29645 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29646 | NO SIGNIFICANT CHANGES OBSERVED |
| 29653 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29663 | NO SIGNIFICANT CHANGES OBSERVED |
| 29666 | NO SIGNIFICANT CHANGES OBSERVED |
| 29667 | NO SIGNIFICANT CHANGES OBSERVED |
| 29668 | NO SIGNIFICANT CHANGES OBSERVED |
| 29673 | NO SIGNIFICANT CHANGES OBSERVED |
| 29675 | NO SIGNIFICANT CHANGES OBSERVED |
| 29685 | NO SIGNIFICANT CHANGES OBSERVED |
| 29698 | NO SIGNIFICANT CHANGES OBSERVED |
| 29710 | NO SIGNIFICANT CHANGES OBSERVED |

TABLE 24
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL DAM GROSS NECROPSY EXAMINATIONS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| DAMS FROM GROUP 3: 300 MG/KG/DAY | MATERNAL GROSS OBSERVATION |
|----------------------------------|---|
| 29592 | NO SIGNIFICANT CHANGES OBSERVED |
| 29596 | NO SIGNIFICANT CHANGES OBSERVED |
| 29607 | FUSED PLACENTA(S) SITES #13 AND #14 |
| 29611 | NO SIGNIFICANT CHANGES OBSERVED |
| 29612 | NO SIGNIFICANT CHANGES OBSERVED |
| 29614 | NO SIGNIFICANT CHANGES OBSERVED |
| 29620 | NO SIGNIFICANT CHANGES OBSERVED |
| 29622 | NO SIGNIFICANT CHANGES OBSERVED |
| 29625 | NO SIGNIFICANT CHANGES OBSERVED |
| 29629 | NO SIGNIFICANT CHANGES OBSERVED |
| 29631 | NO SIGNIFICANT CHANGES OBSERVED |
| 29636 | NO SIGNIFICANT CHANGES OBSERVED |
| 29637 | NO SIGNIFICANT CHANGES OBSERVED |
| 29648 | LUNGS- REDDENED ALL LOBES |
| 29649 | NO SIGNIFICANT CHANGES OBSERVED |
| 29650 | NO SIGNIFICANT CHANGES OBSERVED |
| 29657 | NO SIGNIFICANT CHANGES OBSERVED |
| 29664 | NO SIGNIFICANT CHANGES OBSERVED |
| 29670 | NO SIGNIFICANT CHANGES OBSERVED |
| 29672 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29676 | NO SIGNIFICANT CHANGES OBSERVED |
| 29677 | NO SIGNIFICANT CHANGES OBSERVED |
| 29678 | HAIR LOSS VENTRAL ABDOMINAL; HINDLIMB, RIGHT |
| 29688 | NO SIGNIFICANT CHANGES OBSERVED |
| 29700 | HAIR LOSS HINDLIMB, BILATERAL; RIGHT LATERAL ABDOMINAL |

| DAMS FROM GROUP 4: 1000 MG/KG/DAY | MATERNAL GROSS OBSERVATION |
|-----------------------------------|--|
| 29597 | NO SIGNIFICANT CHANGES OBSERVED |
| 29598 | HAIR LOSS VENTRAL ABDOMINAL; HINDLIMB, LEFT |
| 29608 | NO SIGNIFICANT CHANGES OBSERVED |
| 29613 | NO SIGNIFICANT CHANGES OBSERVED |
| 29616 | NO SIGNIFICANT CHANGES OBSERVED |
| 29618 | KIDNEY- DILATED PELVIS MODERATE, RIGHT |
| 29621 | NO SIGNIFICANT CHANGES OBSERVED |
| 29626 | NO SIGNIFICANT CHANGES OBSERVED |
| 29632 | NO SIGNIFICANT CHANGES OBSERVED |
| 29638 | NO SIGNIFICANT CHANGES OBSERVED |
| 29641 | NO SIGNIFICANT CHANGES OBSERVED |
| 29643 | NO SIGNIFICANT CHANGES OBSERVED |
| 29651 | NO SIGNIFICANT CHANGES OBSERVED |
| 29654 | NO SIGNIFICANT CHANGES OBSERVED LUNGS- REDDENED ALL LOBES |
| 29655 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29658 | NO SIGNIFICANT CHANGES OBSERVED |
| 29659 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE LUNGS- REDDENED ALL LOBES |
| 29665 | NO SIGNIFICANT CHANGES OBSERVED |
| 29671 | NO SIGNIFICANT CHANGES OBSERVED |
| 29679 | NO SIGNIFICANT CHANGES OBSERVED |
| 29680 | NO SIGNIFICANT CHANGES OBSERVED |
| 29681 | NONGRAVID -- AMMONIUM SULFIDE NEGATIVE |
| 29682 | NO SIGNIFICANT CHANGES OBSERVED |
| 29694 | NO SIGNIFICANT CHANGES OBSERVED |
| 29704 | NO SIGNIFICANT CHANGES OBSERVED |

TABLE 25
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL DATA AT THE SCHEDULED NECROPSY

DAMS FROM GROUP 1: 0 MG/KG/DAY

| DAM# | SEX | | VIABLE FETUSES | | | DEAD FETUSES | | | EARLY RESORPTIONS | | | LATE RESORPTIONS | | | IMPLANTATION SITES | | | CORPORA LUTEA | | | | | |
|-------|------|------|----------------|------------|-------|--------------|------------|-------|-------------------|------------|-------|------------------|------------|-------|--------------------|------------|-------|---------------|-------------|-------|------|------|----|
| | M | F | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT OVARY | RIGHT OVARY | TOTAL | | | |
| 29593 | | | NONGRAVID | | | | | | | | | | | | | | | | | | | | |
| 29599 | 10 | 4 | 4 | 10 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 11 | 15 | 5 | 11 | 16 |
| 29601 | 12 | 7 | 10 | 9 | 19 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 11 | 9 | 20 | 11 | 9 | 20 |
| 29602 | 7 | 10 | 5 | 12 | 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 12 | 17 | 10 | 12 | 22 |
| 29609 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 5 | 5 | 10 |
| 29615 | 6 | 7 | 6 | 7 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 7 | 13 | 7 | 7 | 14 |
| 29619 | 5 | 9 | 7 | 7 | 14 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 7 | 9 | 16 | 10 | 9 | 19 |
| 29623 | 9 | 5 | 5 | 9 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 9 | 14 | 5 | 9 | 14 |
| 29628 | 5 | 9 | 7 | 7 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 7 | 14 | 7 | 7 | 14 |
| 29634 | 5 | 10 | 6 | 9 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 9 | 15 | 7 | 9 | 16 |
| 29639 | 8 | 5 | 7 | 6 | 13 | 0 | 0 | 0 | 1 | 1 | 2 | 5 | 0 | 0 | 0 | 0 | 0 | 8 | 7 | 15 | 10 | 9 | 19 |
| 29640 | 4 | 6 | 3 | 7 | 10 | 0 | 0 | 0 | 3 | 2 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 9 | 15 | 6 | 9 | 15 |
| 29644 | 6 | 4 | 1 | 9 | 10 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 10 | 11 | 5 | 11 | 16 |
| 29647 | 8 | 5 | 3 | 10 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 10 | 13 | 3 | 12 | 15 | |
| 29652 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 6 | 3 | 9 |
| 29660 | 12 | 3 | 6 | 9 | 15 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 9 | 16 | 8 | 10 | 18 |
| 29661 | 8 | 5 | 10 | 3 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 10 | 3 | 13 | 10 | 4 | 14 | |
| 29662 | 5 | 8 | 5 | 8 | 13 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 7 | 8 | 15 | 9 | 11 | 20 | |
| 29669 | 8 | 5 | 7 | 6 | 13 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 8 | 7 | 15 | 8 | 8 | 16 | |
| 29674 | 10 | 4 | 10 | 4 | 14 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 11 | 4 | 15 | 11 | 4 | 15 | |
| 29683 | 5 | 8 | 11 | 2 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 11 | 2 | 13 | 11 | 3 | 14 | |
| 29684 | 7 | 6 | 5 | 8 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 8 | 13 | 5 | 9 | 14 | |
| 29695 | 10 | 4 | 9 | 5 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 5 | 14 | 9 | 5 | 14 | |
| 29696 | 6 | 8 | 6 | 8 | 14 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 16 | 9 | 8 | 17 | |
| 29709 | 3 | 8 | 8 | 3 | 11 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 9 | 3 | 12 | 9 | 4 | 13 | |
| TOTAL | 160 | 141 | 143 | 158 | 301 | 0 | 0 | 0 | 13 | 8 | 21 | 0 | 0 | 0 | 0 | 0 | 156 | 166 | 322 | 186 | 188 | 374 | |
| MEAN | 6.7 | 5.9 | 6.0 | 6.6 | 12.5 | 0.0 | 0.0 | 0.0 | 0.5 | 0.3 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.5 | 6.9 | 13.4 | 7.8 | 7.8 | 15.6 | |
| S.D. | 3.06 | 2.63 | 2.88 | 3.17 | 4.02 | 0.00 | 0.00 | 0.00 | 0.83 | 0.64 | 1.19 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 3.02 | 3.32 | 4.23 | 2.35 | 2.85 | 3.03 | |
| | | | | | | | | | | | | | | | | | | | | | | | |

N = 24

TABLE 25
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL DATA AT THE SCHEDULED NECROPSY

DAMS FROM GROUP 2: 30 MG/KG/DAY

| DAM# | SEX | | VIABLE FETUSES | | | DEAD FETUSES | | | EARLY RESORPTIONS | | | LATE RESORPTIONS | | | IMPLANTATION SITES | | | CORPORA LUTEA | | |
|-------|-----------|------|----------------|------------|-------|--------------|------------|-------|-------------------|------------|-------|------------------|------------|-------|--------------------|------------|-------|---------------|-------------|-------|
| | M | F | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT OVARY | RIGHT OVARY | TOTAL |
| 29591 | 5 | 10 | 8 | 7 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 7 | 15 | 8 | 7 | 15 |
| 29595 | 7 | 11 | 7 | 11 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 11 | 18 | 8 | 11 | 19 |
| 29600 | 10 | 7 | 3 | 14 | 17 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 4 | 14 | 18 | 4 | 14 | 18 |
| 29603 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29605 | 2 | 8 | 7 | 3 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 3 | 10 | 8 | 4 | 12 |
| 29606 | 4 | 12 | 7 | 9 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 9 | 16 | 8 | 9 | 17 |
| 29610 | 9 | 6 | 4 | 11 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 11 | 15 | 5 | 12 | 17 |
| 29617 | 5 | 5 | 3 | 7 | 10 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 3 | 9 | 12 | 7 | 10 | 17 |
| 29624 | 9 | 7 | 7 | 9 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 9 | 16 | 7 | 10 | 17 |
| 29630 | 7 | 8 | 9 | 6 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 6 | 15 | 9 | 6 | 15 |
| 29633 | 6 | 10 | 11 | 5 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 11 | 5 | 16 | 11 | 7 | 18 |
| 29635 | 9 | 6 | 4 | 11 | 15 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 5 | 11 | 16 | 5 | 11 | 16 |
| 29642 | 4 | 9 | 5 | 8 | 13 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 5 | 9 | 14 | 7 | 9 | 16 |
| 29645 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29646 | 8 | 13 | 7 | 14 | 21 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 14 | 21 | 9 | 15 | 24 |
| 29653 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29663 | 9 | 8 | 9 | 8 | 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 8 | 17 | 9 | 10 | 19 |
| 29666 | 6 | 5 | 9 | 2 | 11 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 11 | 2 | 13 | 11 | 4 | 15 |
| 29667 | 7 | 6 | 6 | 7 | 13 | 0 | 0 | 0 | 2 | 1 | 3 | 0 | 0 | 0 | 8 | 8 | 16 | 8 | 8 | 16 |
| 29668 | 15 | 3 | 8 | 10 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 10 | 18 | 8 | 11 | 19 |
| 29673 | 11 | 5 | 8 | 8 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 16 | 8 | 9 | 17 |
| 29675 | 4 | 9 | 9 | 4 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 4 | 13 | 10 | 7 | 17 |
| 29685 | 10 | 5 | 7 | 8 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 8 | 15 | 9 | 8 | 17 |
| 29698 | 6 | 7 | 6 | 7 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 7 | 13 | 6 | 8 | 14 |
| 29710 | 6 | 8 | 9 | 5 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 5 | 14 | 9 | 5 | 14 |
| TOTAL | 159 | 168 | 153 | 174 | 327 | 0 | 0 | 0 | 6 | 4 | 10 | 0 | 0 | 0 | 159 | 178 | 337 | 174 | 195 | 369 |
| MEAN | 7.2 | 7.6 | 7.0 | 7.9 | 14.9 | 0.0 | 0.0 | 0.0 | 0.3 | 0.2 | 0.5 | 0.0 | 0.0 | 0.0 | 7.2 | 8.1 | 15.3 | 7.9 | 8.9 | 16.8 |
| S.D. | 2.91 | 2.52 | 2.13 | 3.15 | 2.66 | 0.00 | 0.00 | 0.00 | 0.63 | 0.50 | 0.86 | 0.00 | 0.00 | 0.00 | 2.11 | 3.15 | 2.38 | 1.80 | 2.88 | 2.39 |
| N | = 22 | | | | | | | | | | | | | | | | | | | |

TABLE 25
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL DATA AT THE SCHEDULED NECROPSY

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

DAMS FROM GROUP 3: 300 MG/KG/DAY

| DAM# | SEX | | VIABLE FETUSES | | | DEAD FETUSES | | | EARLY RESORPTIONS | | | LATE RESORPTIONS | | | IMPLANTATION SITES | | | CORPORA LUTEA | | |
|-------|-----------|------|----------------|------------|-------|--------------|------------|-------|-------------------|------------|-------|------------------|------------|-------|--------------------|------------|-------|---------------|-------------|-------|
| | M | F | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT OVARY | RIGHT OVARY | TOTAL |
| 29592 | 9 | 6 | 9 | 6 | 15 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 9 | 7 | 16 | 10 | 7 | 17 |
| 29596 | 4 | 10 | 11 | 3 | 14 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 12 | 3 | 15 | 12 | 8 | 20 |
| 29607 | 5 | 13 | 6 | 12 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 12 | 18 | 6 | 13 | 19 |
| 29611 | 2 | 1 | 3 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 3 | 4 | 8 | 12 |
| 29612 | 3 | 1 | 2 | 2 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 4 | 7 | 9 | 16 |
| 29614 | 8 | 8 | 8 | 8 | 16 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 10 | 8 | 18 | 11 | 8 | 19 |
| 29620 | 2 | 11 | 6 | 7 | 13 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 8 | 7 | 15 | 9 | 9 | 18 |
| 29622 | 7 | 6 | 7 | 6 | 13 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 8 | 6 | 14 | 9 | 7 | 16 |
| 29625 | 14 | 3 | 9 | 8 | 17 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 10 | 8 | 18 | 10 | 9 | 19 |
| 29629 | 6 | 7 | 7 | 6 | 13 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 7 | 8 | 15 | 8 | 8 | 16 |
| 29631 | 10 | 5 | 9 | 6 | 15 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 10 | 6 | 16 | 10 | 7 | 17 |
| 29636 | 4 | 8 | 3 | 9 | 12 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 3 | 10 | 13 | 6 | 14 | 20 |
| 29637 | 5 | 14 | 10 | 9 | 19 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 10 | 10 | 20 | 10 | 11 | 21 |
| 29648 | 3 | 4 | 1 | 6 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 6 | 7 | 5 | 6 | 11 |
| 29649 | 10 | 7 | 9 | 8 | 17 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 9 | 9 | 18 | 9 | 10 | 19 |
| 29650 | 6 | 10 | 8 | 8 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 16 | 10 | 9 | 19 |
| 29657 | 5 | 9 | 7 | 7 | 14 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 7 | 8 | 15 | 9 | 8 | 17 |
| 29664 | 8 | 7 | 7 | 8 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 8 | 15 | 7 | 9 | 16 |
| 29670 | 8 | 8 | 6 | 10 | 16 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 0 | 0 | 7 | 11 | 18 | 9 | 11 | 20 |
| 29672 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29676 | 11 | 7 | 10 | 8 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 10 | 8 | 18 | 10 | 8 | 18 |
| 29677 | 9 | 7 | 6 | 10 | 16 | 0 | 0 | 0 | 1 | 1 | 2 | 0 | 0 | 0 | 7 | 11 | 18 | 9 | 11 | 20 |
| 29678 | 9 | 8 | 7 | 10 | 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 10 | 17 | 8 | 10 | 18 |
| 29688 | 10 | 3 | 5 | 8 | 13 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 5 | 9 | 14 | 5 | 11 | 16 |
| 29700 | 6 | 11 | 9 | 8 | 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 8 | 17 | 10 | 9 | 19 |
| TOTAL | 164 | 174 | 165 | 173 | 338 | 0 | 0 | 0 | 10 | 10 | 20 | 0 | 0 | 0 | 175 | 183 | 358 | 203 | 220 | 423 |
| MEAN | 6.8 | 7.3 | 6.9 | 7.2 | 14.1 | 0.0 | 0.0 | 0.0 | 0.4 | 0.4 | 0.8 | 0.0 | 0.0 | 0.0 | 7.3 | 7.6 | 14.9 | 8.5 | 9.2 | 17.6 |
| S.D. | 3.10 | 3.37 | 2.61 | 2.65 | 4.12 | 0.00 | 0.00 | 0.00 | 0.65 | 0.58 | 0.76 | 0.00 | 0.00 | 0.00 | 2.80 | 2.83 | 4.34 | 2.06 | 1.93 | 2.43 |
| N | = 24 | | | | | | | | | | | | | | | | | | | |

TABLE 25
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL DATA AT THE SCHEDULED NECROPSY

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

DAMS FROM GROUP 4: 1000 MG/KG/DAY

| DAM# | SEX | | VIABLE FETUSES | | | DEAD FETUSES | | | EARLY RESORPTIONS | | | LATE RESORPTIONS | | | IMPLANTATION SITES | | | CORPORA LUTEA | | |
|-------|-----------|------|----------------|------------|-------|--------------|------------|-------|-------------------|------------|-------|------------------|------------|-------|--------------------|------------|-------|---------------|-------------|-------|
| | M | F | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT HORN | RIGHT HORN | TOTAL | LEFT OVARY | RIGHT OVARY | TOTAL |
| 29597 | 3 | 6 | 0 | 9 | 9 | 0 | 0 | 0 | 1 | 2 | 3 | 0 | 0 | 0 | 1 | 11 | 12 | 1 | 12 | 13 |
| 29598 | 8 | 5 | 9 | 4 | 13 | 0 | 0 | 0 | 2 | 1 | 3 | 0 | 0 | 0 | 11 | 5 | 16 | 11 | 5 | 16 |
| 29608 | 10 | 3 | 5 | 8 | 13 | 0 | 0 | 0 | 1 | 2 | 3 | 0 | 0 | 0 | 6 | 10 | 16 | 10 | 15 | 25 |
| 29613 | 7 | 8 | 7 | 8 | 15 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 8 | 8 | 16 | 8 | 9 | 17 |
| 29616 | 8 | 7 | 10 | 5 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 10 | 5 | 15 | 10 | 9 | 19 |
| 29618 | 9 | 6 | 8 | 7 | 15 | 0 | 0 | 0 | 2 | 0 | 2 | 0 | 0 | 0 | 10 | 7 | 17 | 10 | 8 | 18 |
| 29621 | 7 | 8 | 7 | 8 | 15 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 8 | 8 | 16 | 8 | 8 | 16 |
| 29626 | 4 | 8 | 6 | 6 | 12 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 7 | 6 | 13 | 8 | 6 | 14 |
| 29632 | 6 | 7 | 5 | 8 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 8 | 13 | 6 | 8 | 14 |
| 29638 | 11 | 4 | 5 | 10 | 15 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 6 | 10 | 16 | 6 | 10 | 16 |
| 29641 | 9 | 5 | 6 | 8 | 14 | 0 | 0 | 0 | 1 | 3 | 4 | 0 | 0 | 0 | 7 | 11 | 18 | 8 | 11 | 19 |
| 29643 | 10 | 8 | 9 | 9 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 9 | 18 | 10 | 9 | 19 |
| 29651 | 13 | 5 | 9 | 9 | 18 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 9 | 18 | 11 | 10 | 21 |
| 29654 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29655 | 5 | 7 | 5 | 7 | 12 | 0 | 0 | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 5 | 10 | 15 | 5 | 12 | 17 |
| 29658 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29659 | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 6 | 4 | 10 |
| 29665 | 7 | 6 | 8 | 5 | 13 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 5 | 13 | 8 | 5 | 13 |
| 29671 | 6 | 8 | 5 | 9 | 14 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 5 | 10 | 15 | 7 | 12 | 19 |
| 29679 | 6 | 10 | 8 | 8 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 16 | 12 | 9 | 21 |
| 29680 | 7 | 9 | 7 | 9 | 16 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 8 | 9 | 17 | 9 | 9 | 18 |
| 29681 | NONGRAVID | | | | | | | | | | | | | | | | | | | |
| 29682 | 9 | 5 | 9 | 5 | 14 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 10 | 5 | 15 | 11 | 9 | 20 |
| 29694 | 8 | 9 | 8 | 9 | 17 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 9 | 17 | 8 | 10 | 18 |
| 29704 | 10 | 5 | 8 | 7 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 7 | 15 | 8 | 8 | 16 |
| TOTAL | 165 | 139 | 144 | 160 | 304 | 0 | 0 | 0 | 12 | 12 | 24 | 1 | 0 | 1 | 157 | 172 | 329 | 181 | 198 | 379 |
| MEAN | 7.5 | 6.3 | 6.5 | 7.3 | 13.8 | 0.0 | 0.0 | 0.0 | 0.5 | 0.5 | 1.1 | 0.0 | 0.0 | 0.0 | 7.1 | 7.8 | 15.0 | 8.2 | 9.0 | 17.2 |
| S.D. | 2.63 | 2.28 | 2.63 | 2.00 | 3.35 | 0.00 | 0.00 | 0.00 | 0.67 | 1.01 | 1.31 | 0.21 | 0.00 | 0.21 | 2.73 | 2.34 | 3.34 | 2.49 | 2.58 | 3.28 |
| N | = 22 | | | | | | | | | | | | | | | | | | | |

TABLE 26

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY (% PER LITTER)

DAMS FROM GROUP 1: 0 MG/KG/DAY

| DAM # | CORPORA LUTEA | IMPLANTATION SITES | FETUSES | | RESORPTIONS | | PRE- IMPLANTATION | | POST- IMPLANTATION | | MALES | FEMALES |
|-------|------------------|-----------------------|---------|------|-------------|------|----------------------|------|-----------------------|------|-------|---------|
| | | | VIABLE | DEAD | EARLY | LATE | TOTAL | LOSS | LOSS | LOSS | | |
| | # | # | % | % | % | % | % | % | % | % | % | % |
| 29599 | 16.0 | 15.0 | 93.3 | 0.0 | 6.7 | 0.0 | 6.7 | 0.0 | 6.7 | 6.7 | 71.4 | 28.6 |
| 29601 | 20.0 | 20.0 | 95.0 | 0.0 | 5.0 | 0.0 | 5.0 | 0.0 | 5.0 | 5.0 | 63.2 | 36.8 |
| 29602 | 22.0 | 17.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 22.7 | 0.0 | 41.2 | 58.8 |
| 29609 | 10.0 | 1.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 90.0 | 0.0 | 100.0 | 0.0 |
| 29615 | 14.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 46.2 | 53.8 |
| 29619 | 19.0 | 16.0 | 87.5 | 0.0 | 12.5 | 0.0 | 12.5 | 0.0 | 15.8 | 12.5 | 35.7 | 64.3 |
| 29623 | 14.0 | 14.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 64.3 | 35.7 |
| 29628 | 14.0 | 14.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 35.7 | 64.3 |
| 29634 | 16.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.3 | 0.0 | 33.3 | 66.7 |
| 29639 | 19.0 | 15.0 | 86.7 | 0.0 | 13.3 | 0.0 | 13.3 | 0.0 | 21.1 | 13.3 | 61.5 | 38.5 |
| 29640 | 15.0 | 15.0 | 66.7 | 0.0 | 33.3 | 0.0 | 33.3 | 0.0 | 0.0 | 33.3 | 40.0 | 60.0 |
| 29644 | 16.0 | 11.0 | 90.9 | 0.0 | 9.1 | 0.0 | 9.1 | 0.0 | 31.3 | 9.1 | 60.0 | 40.0 |
| 29647 | 15.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 13.3 | 0.0 | 61.5 | 38.5 |
| 29652 | 9.0 | 1.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 88.9 | 0.0 | 0.0 | 100.0 |
| 29660 | 18.0 | 16.0 | 93.8 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 11.1 | 6.3 | 80.0 | 20.0 |
| 29661 | 14.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 61.5 | 38.5 |
| 29662 | 20.0 | 15.0 | 86.7 | 0.0 | 13.3 | 0.0 | 13.3 | 0.0 | 25.0 | 13.3 | 38.5 | 61.5 |
| 29669 | 16.0 | 15.0 | 86.7 | 0.0 | 13.3 | 0.0 | 13.3 | 0.0 | 6.3 | 13.3 | 61.5 | 38.5 |
| 29674 | 15.0 | 15.0 | 93.3 | 0.0 | 6.7 | 0.0 | 6.7 | 0.0 | 0.0 | 6.7 | 71.4 | 28.6 |
| 29683 | 14.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 38.5 | 61.5 |
| 29684 | 14.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 53.8 | 46.2 |
| 29695 | 14.0 | 14.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 71.4 | 28.6 |
| 29696 | 17.0 | 16.0 | 87.5 | 0.0 | 12.5 | 0.0 | 12.5 | 0.0 | 5.9 | 12.5 | 42.9 | 57.1 |
| 29709 | 13.0 | 12.0 | 91.7 | 0.0 | 8.3 | 0.0 | 8.3 | 0.0 | 7.7 | 8.3 | 27.3 | 72.7 |
| MEAN | 15.6 | 13.4 | 94.2 | 0.0 | 5.8 | 0.0 | 5.8 | 0.0 | 15.8 | 5.8 | 52.5 | 47.5 |
| S.D. | 3.03 | 4.23 | 7.91 | 0.00 | 7.91 | 0.00 | 7.91 | 0.00 | 24.24 | 7.91 | 20.70 | 20.70 |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |

TABLE 26
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY (% PER LITTER)

DAMS FROM GROUP 2: 30 MG/KG/DAY

| DAM # | CORPORA LUTEA | IMPLANTATION SITES | | FETUSES VIABLE | | DEAD | | RESORPTIONS | | TOTAL | | PRE-IMPLANTATION LOSS | | POST-IMPLANTATION LOSS | | MALES | | FEMALES | |
|-------|---------------|--------------------|-------|----------------|------|------|------|-------------|------|-------|------|-----------------------|------|------------------------|------|-------|-------|---------|---|
| | | # | % | # | % | # | % | # | % | EARLY | LATE | % | % | % | % | % | % | % | % |
| 29591 | 15.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 33.3 | 66.7 | | |
| 29595 | 19.0 | 18.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.3 | 0.0 | 0.0 | 0.0 | 38.9 | 61.1 | | |
| 29600 | 18.0 | 18.0 | 94.4 | 0.0 | 0.0 | 5.6 | 0.0 | 0.0 | 0.0 | 5.6 | 0.0 | 0.0 | 0.0 | 5.6 | 0.0 | 58.8 | 41.2 | | |
| 29605 | 12.0 | 10.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 16.7 | 0.0 | 0.0 | 0.0 | 20.0 | 80.0 | | |
| 29606 | 17.0 | 16.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.9 | 0.0 | 0.0 | 0.0 | 25.0 | 75.0 | | |
| 29610 | 17.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 11.8 | 0.0 | 0.0 | 0.0 | 60.0 | 40.0 | | |
| 29617 | 17.0 | 12.0 | 83.3 | 0.0 | 0.0 | 16.7 | 0.0 | 0.0 | 0.0 | 16.7 | 0.0 | 29.4 | 0.0 | 16.7 | 0.0 | 50.0 | 50.0 | | |
| 29624 | 17.0 | 16.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.9 | 0.0 | 0.0 | 0.0 | 56.3 | 43.8 | | |
| 29630 | 15.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 46.7 | 53.3 | | |
| 29633 | 18.0 | 16.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 11.1 | 0.0 | 0.0 | 0.0 | 37.5 | 62.5 | | |
| 29635 | 16.0 | 16.0 | 93.8 | 0.0 | 0.0 | 6.3 | 0.0 | 0.0 | 0.0 | 6.3 | 0.0 | 0.0 | 0.0 | 6.3 | 0.0 | 60.0 | 40.0 | | |
| 29642 | 16.0 | 14.0 | 92.9 | 0.0 | 0.0 | 7.1 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 12.5 | 0.0 | 7.1 | 0.0 | 30.8 | 69.2 | | |
| 29646 | 24.0 | 21.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 12.5 | 0.0 | 0.0 | 0.0 | 38.1 | 61.9 | | |
| 29663 | 19.0 | 17.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 10.5 | 0.0 | 0.0 | 0.0 | 52.9 | 47.1 | | |
| 29666 | 15.0 | 13.0 | 84.6 | 0.0 | 0.0 | 15.4 | 0.0 | 0.0 | 0.0 | 15.4 | 0.0 | 13.3 | 0.0 | 15.4 | 0.0 | 54.5 | 45.5 | | |
| 29667 | 16.0 | 16.0 | 81.3 | 0.0 | 0.0 | 18.8 | 0.0 | 0.0 | 0.0 | 18.8 | 0.0 | 0.0 | 0.0 | 18.8 | 0.0 | 53.8 | 46.2 | | |
| 29668 | 19.0 | 18.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.3 | 0.0 | 0.0 | 0.0 | 83.3 | 16.7 | | |
| 29673 | 17.0 | 16.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.9 | 0.0 | 0.0 | 0.0 | 68.8 | 31.3 | | |
| 29675 | 17.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 23.5 | 0.0 | 0.0 | 0.0 | 30.8 | 69.2 | | |
| 29685 | 17.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 11.8 | 0.0 | 0.0 | 0.0 | 66.7 | 33.3 | | |
| 29698 | 14.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 0.0 | 0.0 | 46.2 | 53.8 | | |
| 29710 | 14.0 | 14.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 42.9 | 57.1 | | |
| MEAN | 16.8 | 15.3 | 96.8 | 0.0 | 0.0 | 3.2 | 0.0 | 0.0 | 0.0 | 3.2 | 0.0 | 8.6 | 0.0 | 3.2 | 0.0 | 48.0 | 52.0 | | |
| S.D. | 2.39 | 2.38 | 6.04 | 0.00 | 0.00 | 6.05 | 0.00 | 0.00 | 0.00 | 6.05 | 0.00 | 7.85 | 0.00 | 6.05 | 0.00 | 15.51 | 15.50 | | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | |

TABLE 26
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY (% PER LITTER)

DAMS FROM GROUP 3: 300 MG/KG/DAY

| DAM # | CORPORA LUTEA | IMPLANTATION SITES | | FETUSES VIABLE | | DEAD | | RESORPTIONS | | TOTAL | | PRE-IMPLANTATION LOSS | | POST-IMPLANTATION LOSS | | MALES | | FEMALES | |
|-------|---------------|--------------------|-------|----------------|------|------|------|-------------|------|-------|-------|-----------------------|-------|------------------------|---|-------|---|---------|---|
| | | # | % | # | % | # | % | # | % | EARLY | LATE | % | % | % | % | % | % | % | % |
| 29592 | 17.0 | 16.0 | 93.8 | 0.0 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 6.3 | 5.9 | 6.3 | 60.0 | 40.0 | | | | | |
| 29596 | 20.0 | 15.0 | 93.3 | 0.0 | 0.0 | 6.7 | 0.0 | 6.7 | 0.0 | 6.7 | 25.0 | 6.7 | 28.6 | 71.4 | | | | | |
| 29607 | 19.0 | 18.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.3 | 0.0 | 27.8 | 72.2 | | | | | |
| 29611 | 12.0 | 3.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 75.0 | 0.0 | 66.7 | 33.3 | | | | | |
| 29612 | 16.0 | 4.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 75.0 | 0.0 | 75.0 | 25.0 | | | | | |
| 29614 | 19.0 | 18.0 | 88.9 | 0.0 | 0.0 | 11.1 | 0.0 | 11.1 | 0.0 | 11.1 | 5.3 | 11.1 | 50.0 | 50.0 | | | | | |
| 29620 | 18.0 | 15.0 | 86.7 | 0.0 | 0.0 | 13.3 | 0.0 | 13.3 | 0.0 | 13.3 | 16.7 | 13.3 | 15.4 | 84.6 | | | | | |
| 29622 | 16.0 | 14.0 | 92.9 | 0.0 | 0.0 | 7.1 | 0.0 | 7.1 | 0.0 | 7.1 | 12.5 | 7.1 | 53.8 | 46.2 | | | | | |
| 29625 | 19.0 | 18.0 | 94.4 | 0.0 | 0.0 | 5.6 | 0.0 | 5.6 | 0.0 | 5.6 | 5.3 | 5.6 | 82.4 | 17.6 | | | | | |
| 29629 | 16.0 | 15.0 | 86.7 | 0.0 | 0.0 | 13.3 | 0.0 | 13.3 | 0.0 | 13.3 | 6.3 | 13.3 | 46.2 | 53.8 | | | | | |
| 29631 | 17.0 | 16.0 | 93.8 | 0.0 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 6.3 | 5.9 | 6.3 | 66.7 | 33.3 | | | | | |
| 29636 | 20.0 | 13.0 | 92.3 | 0.0 | 0.0 | 7.7 | 0.0 | 7.7 | 0.0 | 7.7 | 35.0 | 7.7 | 33.3 | 66.7 | | | | | |
| 29637 | 21.0 | 20.0 | 95.0 | 0.0 | 0.0 | 5.0 | 0.0 | 5.0 | 0.0 | 5.0 | 4.8 | 5.0 | 26.3 | 73.7 | | | | | |
| 29648 | 11.0 | 7.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 36.4 | 0.0 | 42.9 | 57.1 | | | | | |
| 29649 | 19.0 | 18.0 | 94.4 | 0.0 | 0.0 | 5.6 | 0.0 | 5.6 | 0.0 | 5.6 | 5.3 | 5.6 | 58.8 | 41.2 | | | | | |
| 29650 | 19.0 | 16.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 15.8 | 0.0 | 37.5 | 62.5 | | | | | |
| 29657 | 17.0 | 15.0 | 93.3 | 0.0 | 0.0 | 6.7 | 0.0 | 6.7 | 0.0 | 6.7 | 11.8 | 6.7 | 35.7 | 64.3 | | | | | |
| 29664 | 16.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.3 | 0.0 | 53.3 | 46.7 | | | | | |
| 29670 | 20.0 | 18.0 | 88.9 | 0.0 | 0.0 | 11.1 | 0.0 | 11.1 | 0.0 | 11.1 | 10.0 | 11.1 | 50.0 | 50.0 | | | | | |
| 29676 | 18.0 | 18.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 61.1 | 38.9 | | | | | |
| 29677 | 20.0 | 18.0 | 88.9 | 0.0 | 0.0 | 11.1 | 0.0 | 11.1 | 0.0 | 11.1 | 10.0 | 11.1 | 56.3 | 43.8 | | | | | |
| 29678 | 18.0 | 17.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.6 | 0.0 | 52.9 | 47.1 | | | | | |
| 29688 | 16.0 | 14.0 | 92.9 | 0.0 | 0.0 | 7.1 | 0.0 | 7.1 | 0.0 | 7.1 | 12.5 | 7.1 | 76.9 | 23.1 | | | | | |
| 29700 | 19.0 | 17.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 10.5 | 0.0 | 35.3 | 64.7 | | | | | |
| MEAN | 17.6 | 14.9 | 94.8 | 0.0 | 0.0 | 5.2 | 0.0 | 5.2 | 0.0 | 5.2 | 16.8 | 5.2 | 49.7 | 50.3 | | | | | |
| S.D. | 2.43 | 4.34 | 4.66 | 0.00 | 0.00 | 4.66 | 0.00 | 4.66 | 0.00 | 4.66 | 20.10 | 4.66 | 17.39 | 17.39 | | | | | |
| N | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | | | | | |

TABLE 26
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY (% PER LITTER)

PROJECT NO.: WIL-15218
SPONSOR: VELSITCOL

DAMS FROM GROUP 4: 1000 MG/KG/DAY

| DAM # | CORPORA LUTEA | IMPLANTATION SITES | | FETUSES VIABLE | | FETUSES DEAD | | RESORPTIONS | | PRE-IMPLANTATION LOSS | | POST-IMPLANTATION LOSS | | MALES | | FEMALES | |
|-------|---------------|--------------------|-------|----------------|------|--------------|------|-------------|------|-----------------------|-------|------------------------|-------|-------|-------|---------|---|
| | | # | % | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
| 29597 | 13.0 | 12.0 | 75.0 | 0.0 | 0.0 | 25.0 | 0.0 | 25.0 | 0.0 | 25.0 | 7.7 | 25.0 | 33.3 | 66.7 | 33.3 | 66.7 | |
| 29598 | 16.0 | 16.0 | 81.3 | 0.0 | 0.0 | 18.8 | 0.0 | 18.8 | 0.0 | 18.8 | 0.0 | 18.8 | 61.5 | 38.5 | 61.5 | 38.5 | |
| 29608 | 25.0 | 16.0 | 81.3 | 0.0 | 0.0 | 18.8 | 0.0 | 18.8 | 0.0 | 18.8 | 36.0 | 18.8 | 76.9 | 23.1 | 76.9 | 23.1 | |
| 29613 | 17.0 | 16.0 | 93.8 | 0.0 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 6.3 | 5.9 | 6.3 | 46.7 | 53.3 | 46.7 | 53.3 | |
| 29616 | 19.0 | 15.0 | 100.0 | 0.0 | 0.0 | 11.8 | 0.0 | 11.8 | 0.0 | 11.8 | 21.1 | 0.0 | 53.3 | 46.7 | 53.3 | 46.7 | |
| 29618 | 18.0 | 17.0 | 88.2 | 0.0 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 6.3 | 5.6 | 11.8 | 60.0 | 40.0 | 60.0 | 40.0 | |
| 29621 | 16.0 | 16.0 | 93.8 | 0.0 | 0.0 | 7.7 | 0.0 | 7.7 | 0.0 | 6.3 | 0.0 | 6.3 | 46.7 | 53.3 | 46.7 | 53.3 | |
| 29626 | 14.0 | 13.0 | 92.3 | 0.0 | 0.0 | 7.7 | 0.0 | 7.7 | 0.0 | 7.7 | 7.1 | 7.7 | 33.3 | 66.7 | 33.3 | 66.7 | |
| 29632 | 14.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.1 | 0.0 | 46.2 | 53.8 | 46.2 | 53.8 | |
| 29638 | 16.0 | 16.0 | 93.8 | 0.0 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 6.3 | 0.0 | 6.3 | 73.3 | 26.7 | 73.3 | 26.7 | |
| 29641 | 19.0 | 18.0 | 77.8 | 0.0 | 0.0 | 22.2 | 0.0 | 22.2 | 0.0 | 22.2 | 5.3 | 22.2 | 64.3 | 35.7 | 64.3 | 35.7 | |
| 29643 | 19.0 | 18.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.3 | 0.0 | 55.6 | 44.4 | 55.6 | 44.4 | |
| 29651 | 21.0 | 18.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 14.3 | 0.0 | 72.2 | 27.8 | 72.2 | 27.8 | |
| 29655 | 17.0 | 15.0 | 80.0 | 0.0 | 0.0 | 20.0 | 0.0 | 20.0 | 0.0 | 20.0 | 11.8 | 20.0 | 41.7 | 58.3 | 41.7 | 58.3 | |
| 29659 | 10.0 | 2.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 80.0 | 0.0 | 100.0 | 0.0 | 100.0 | 0.0 | |
| 29665 | 13.0 | 13.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 53.8 | 46.2 | 53.8 | 46.2 | |
| 29671 | 19.0 | 15.0 | 93.3 | 0.0 | 0.0 | 6.7 | 0.0 | 6.7 | 0.0 | 6.7 | 21.1 | 6.7 | 42.9 | 57.1 | 42.9 | 57.1 | |
| 29679 | 21.0 | 16.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 23.8 | 0.0 | 37.5 | 62.5 | 37.5 | 62.5 | |
| 29680 | 18.0 | 17.0 | 94.1 | 0.0 | 0.0 | 5.9 | 0.0 | 5.9 | 0.0 | 5.9 | 5.6 | 5.9 | 43.8 | 56.3 | 43.8 | 56.3 | |
| 29682 | 20.0 | 15.0 | 93.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.7 | 25.0 | 6.7 | 64.3 | 35.7 | 64.3 | 35.7 | |
| 29694 | 18.0 | 17.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 5.6 | 0.0 | 47.1 | 52.9 | 47.1 | 52.9 | |
| 29704 | 16.0 | 15.0 | 100.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.3 | 0.0 | 66.7 | 33.3 | 66.7 | 33.3 | |
| MEAN | 17.2 | 15.0 | 92.6 | 0.0 | 0.0 | 7.1 | 0.3 | 7.4 | 0.3 | 7.4 | 13.4 | 7.4 | 55.5 | 44.5 | 55.5 | 44.5 | |
| S.D. | 3.28 | 3.34 | 8.35 | 0.00 | 0.00 | 8.50 | 1.43 | 8.36 | 1.43 | 8.36 | 17.68 | 8.36 | 16.16 | 16.17 | 16.16 | 16.17 | |
| N | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | 22 | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL WEIGHTS (GRAMS)

PROJECT NO.: WIL-15218
SPONSOR: VELSICOL

| FETUS # | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
|---------|----------------|------|-----|------|------|------|------|------|------|------|------|------|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|
| DAM # | MEAN | | | | | | | | | | | | | | | | | | | | | | |
| GROUP | 1: 0 MG/KG/DAY | | | | | | | | | | | | | | | | | | | | | | |
| 29599 | 3.5 | 3.4 | 3.5 | 3.8/ | 3.6 | 3.5 | E | 3.4 | 3.4 | 3.2 | 3.7 | 3.6 | 3.7 | 3.4 | 3.3 | | | | | | | | |
| 29601 | 3.5 | 3.4 | 3.3 | E | 3.4 | 3.8 | 3.0 | 3.2 | 3.7 | 3.4 | 3.6/ | 3.6 | 3.7 | 3.6 | 4.0 | 3.7 | 3.6 | 3.4 | 3.5 | 3.5 | | | |
| 29602 | 3.0 | 2.8 | 3.0 | 3.2 | 3.5/ | 3.3 | 3.2 | 3.3 | 3.5 | 3.3 | 3.1 | 3.4 | 3.2 | 3.2 | 3.6 | 3.4 | 3.0 | | | | | | |
| 29609 | 4.0 | 4.0/ | | | | | | | | | | | | | | | | | | | | | |
| 29615 | 3.8 | 3.7 | 3.8 | 4.0 | 4.0 | 3.9/ | 4.0 | 3.9 | 4.0 | 3.6 | 3.6 | 3.7 | 3.8 | | | | | | | | | | |
| 29619 | 3.3 | 3.4 | 3.5 | 3.5 | 3.4 | 3.8 | 3.7/ | E | 3.2 | 3.4 | 3.3 | 3.7 | 3.9 | E | 3.9 | 3.6 | | | | | | | |
| 29623 | 3.5 | 3.2 | 3.1 | 3.4 | 3.4/ | 3.9 | 3.5 | 3.5 | 3.4 | 3.8 | 3.8 | 3.6 | 3.1 | 3.2 | | | | | | | | | |
| 29628 | 3.6 | 3.5 | 3.2 | 3.1 | 3.5 | 3.7 | 3.9 | 4.1/ | 3.9 | 3.3 | 3.7 | 3.9 | 3.7 | 3.3 | | | | | | | | | |
| 29634 | 3.7 | 3.6 | 4.0 | 3.8 | 3.7 | 4.1 | 3.7/ | 3.6 | 3.9 | 3.5 | 3.3 | 3.8 | 3.8 | 3.7 | 3.6 | 3.7 | | | | | | | |
| 29639 | 3.5 | 3.3 | 3.3 | E | 3.8 | 3.6 | 4.1 | 3.5 | 3.9/ | 3.4 | E | 3.3 | 3.5 | 3.2 | 3.5 | 3.5 | | | | | | | |
| 29640 | 3.3 | E | 3.4 | 3.6 | 3.1 | E/ | 2.5 | 3.1 | 3.9 | E | 3.6 | 3.2 | 3.4 | E | 3.5 | 3.6 | | | | | | | |
| 29644 | 3.5 | 3.9/ | 3.5 | 3.7 | 3.8 | 3.5 | 3.4 | 3.7 | E | 3.0 | 3.1 | 3.2 | | | | | | | | | | | |
| 29647 | 3.1 | 3.1 | 3.0 | 2.7/ | 3.3 | 3.5 | 3.2 | 2.8 | 3.3 | 2.9 | 3.3 | 3.3 | 3.1 | | | | | | | | | | |
| 29652 | 4.1 | 4.1/ | | | | | | | | | | | | | | | | | | | | | |
| 29660 | 3.3 | 3.2 | 3.3 | 3.7 | 3.2 | 3.5 | E | 3.4/ | 3.1 | 3.4 | 3.4 | 3.4 | 3.2 | 3.3 | 3.3 | 3.3 | 2.9 | | | | | | |
| 29661 | 3.7 | 3.9 | 3.4 | 3.8 | 3.7 | 3.6 | 3.8 | 3.8 | 3.7 | 3.8 | 3.8/ | 4.0 | 3.6 | 3.7 | | | | | | | | | |
| 29662 | 3.8 | 3.9 | E | 3.7 | 3.6 | 4.0 | 3.7/ | 3.6 | 3.7 | 3.9 | 3.5 | 3.9 | 4.0 | 3.8 | 3.5 | | | | | | | | |
| 29669 | 3.6 | 3.3 | 3.7 | 3.5 | 4.3 | 3.5 | 3.5 | E | 3.7/ | 3.3 | 3.5 | 3.6 | 3.8 | 3.5 | 3.7 | E | | | | | | | |
| 29674 | 3.6 | 3.5 | 3.2 | 3.6 | 3.8 | 3.8 | 3.5 | 3.8 | E | 2.9 | 3.4 | 3.9/ | 3.7 | 3.7 | 3.6 | 3.7 | | | | | | | |
| 29683 | 3.4 | 3.6 | 3.8 | 3.4 | 3.5 | 3.2 | 3.4 | 3.0 | 3.9 | 2.9 | 3.5 | 3.4/ | 3.5 | 2.6 | | | | | | | | | |
| 29684 | 3.3 | 3.6 | 3.5 | 3.4 | 3.3/ | 3.2 | 3.1 | 3.4 | 3.0 | 3.2 | 3.4 | 3.1 | 3.0 | | | | | | | | | | |
| 29695 | 3.7 | 2.8 | 3.5 | 3.4 | 4.1 | 3.7 | 3.5 | 3.8 | 4.0 | 4.1/ | 3.9 | 3.4 | 3.6 | 3.7 | 3.6 | | | | | | | | |
| 29696 | 3.9 | 3.8 | E | 3.8 | 3.7 | 3.9 | 4.1 | 3.9/ | 3.9 | 3.7 | 4.0 | 3.6 | 4.0 | 3.9 | 4.0 | 3.8 | | | | | | | |
| 29709 | 3.7 | 3.7 | 3.9 | 4.0 | 3.4 | E | 3.7 | 3.6 | 3.8 | 3.8/ | 3.3 | 3.8 | 3.8 | | | | | | | | | | |

MEAN 3.6
S.D. 0.25
N 24

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

| FETUS # | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | |
|---------|-----------------|-----|------|------|------|-----|------|------|------|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|--|
| DAM # | MEAN | | | | | | | | | | | | | | | | | | | | | | | |
| GROUP | 2: 30 MG/KG/DAY | | | | | | | | | | | | | | | | | | | | | | | |
| 29591 | 3.1 | 3.2 | 3.4 | 2.9 | 3.1 | 3.2 | 3.2 | 3.6/ | 3.4 | 3.3 | 3.2 | 3.1 | 3.2 | 3.0 | 3.0 | | | | | | | | | |
| 29595 | 3.1 | 3.0 | 3.5 | 2.9 | 3.1 | 3.6 | 3.7/ | 3.3 | 2.9 | 3.1 | 3.3 | 3.1 | 3.3 | 3.3 | 3.3 | 3.4 | 3.7 | 3.4 | | | | | | |
| 29600 | E | 3.7 | 4.0 | 3.5/ | 3.2 | 3.3 | 3.1 | 2.3 | 3.7 | 3.5 | 3.7 | 3.4 | 3.5 | 3.4 | 3.5 | 3.4 | 3.2 | 2.8 | | | | | | |
| 29605 | 3.1 | 3.4 | 3.6 | 3.0 | 3.4 | 3.8 | 3.4/ | 2.9 | 3.6 | 3.6 | | | | | | | | | | | | | | |
| 29606 | 3.6 | 3.8 | 3.9 | 3.8 | 3.5 | 3.7 | 3.4/ | 3.5 | 3.7 | 3.5 | 3.8 | 3.8 | 3.7 | 3.7 | 3.6 | 3.5 | | | | | | | | |
| 29610 | 3.8 | 3.4 | 3.4 | 3.4/ | 3.4 | 3.3 | 3.3 | 3.4 | 3.6 | 2.2 | 3.3 | 3.5 | 3.4 | 3.1 | 3.1 | | | | | | | | | |
| 29617 | 3.5 | 3.2 | 3.6/ | E | 3.0 | 3.4 | 3.6 | E | 3.7 | 3.3 | 3.5 | 3.0 | | | | | | | | | | | | |
| 29624 | 2.6 | 3.2 | 3.3 | 3.2 | 3.4 | 3.2 | 3.0/ | 3.1 | 3.5 | 3.3 | 3.5 | 3.5 | 3.7 | 3.1 | 3.3 | 2.1 | | | | | | | | |
| 29630 | 3.4 | 3.3 | 3.8 | 3.7 | 3.7 | 4.0 | 3.5 | 3.7 | 3.6/ | 3.4 | 3.8 | 3.8 | 3.3 | 3.7 | 3.2 | | | | | | | | | |
| 29633 | 3.1 | 3.0 | 2.9 | 3.5 | 3.0 | 2.7 | 3.2 | 3.0 | 3.1 | 3.0 | 3.0/ | 3.2 | 3.3 | 3.5 | 3.2 | 3.3 | | | | | | | | |
| 29635 | 3.6 | 3.5 | 3.6 | 3.9 | 4.0/ | 3.3 | 3.5 | 3.4 | 3.8 | 3.4 | 3.5 | 3.9 | 3.8 | 3.3 | 3.9 | 3.4 | | | | | | | | |
| 29642 | 3.3 | 3.0 | 2.9 | 3.3 | 3.8/ | 3.1 | 2.9 | 2.9 | 3.3 | 3.2 | 3.1 | E | 3.3 | 2.9 | | | | | | | | | | |
| 29646 | 3.4 | 3.3 | 3.4 | 3.4 | 3.3 | 3.4 | 3.4/ | 3.4 | 3.6 | 3.4 | 3.4 | 3.6 | 3.0 | 3.6 | 3.3 | 2.8 | 3.0 | 3.3 | 3.6 | 2.9 | 3.1 | | | |
| 29663 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.6 | 3.6 | 3.6 | 3.6/ | 3.3 | 3.4 | 3.6 | 3.6 | 3.5 | 3.5 | 3.3 | 3.4 | | | | | | | |
| 29666 | 3.5 | 3.7 | 2.3 | 3.7 | 3.2 | 3.5 | 3.7 | 3.5 | E | 3.7 | 3.5/ | 3.6 | 3.7 | | | | | | | | | | | |
| 29667 | 3.8 | 3.4 | 3.6 | 3.6 | 3.6 | E | 4.0 | E/ | 3.9 | 3.6 | E | 3.6 | 3.9 | 3.8 | 3.4 | 3.3 | | | | | | | | |
| 29668 | 3.3 | 3.5 | 3.5 | 2.7 | 3.4 | 3.4 | 3.2 | 3.5/ | 3.0 | 3.4 | 3.3 | 3.5 | 3.5 | 3.2 | 3.3 | 3.6 | 3.0 | 3.1 | | | | | | |
| 29673 | 3.6 | 3.6 | 3.9 | 3.6 | 3.2 | 3.4 | 3.5 | 3.9/ | 3.6 | 3.4 | 3.8 | 3.7 | 3.8 | 3.5 | 3.3 | 3.7 | | | | | | | | |
| 29675 | 3.7 | 3.5 | 4.1 | 3.9 | 3.5 | 3.6 | 3.7 | 3.5 | 3.8 | 3.7 | 3.4 | 3.9 | 3.8 | | | | | | | | | | | |
| 29685 | 3.6 | 3.7 | 3.6 | 3.8 | 3.5 | 3.7 | 3.2 | 3.6/ | 3.8 | 3.5 | 3.6 | 3.5 | 3.6 | 3.3 | 3.5 | 3.5 | | | | | | | | |
| 29698 | 3.5 | 3.4 | 3.5 | 3.4 | 3.6 | 3.7 | 3.5/ | 3.9 | 3.7 | 3.9 | 3.5 | 2.7 | 3.4 | | | | | | | | | | | |
| 29710 | 3.0 | 3.2 | 3.3 | 3.5 | 3.4 | 3.1 | 3.1 | 3.3 | 3.6/ | 3.2 | 3.3 | 3.4 | 3.3 | 3.4 | | | | | | | | | | |

MEAN 3.4
S.D. 0.18
N 22

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

TABLE 27
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL WEIGHTS (GRAMS)

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

| FETUS # | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
|---------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
|---------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|

| DAM # | MEAN | GROUP | 3: 300 MG/KG/DAY | | | | | | | | | | | | | | | | | | | | | | |
|-------|------|-------|------------------|------|-----|------|------|------|------|------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|
| 29592 | 3.8 | 3.6 | 4.0 | 3.6 | 3.8 | 4.0 | 4.0 | 3.6 | 4.0 | 3.8/ | 4.0 | 4.2 | E | 3.6 | 3.7 | 3.5 | 3.5 | | | | | | | | |
| 29596 | 3.5 | 3.5 | 3.4 | 3.6 | 3.3 | 3.6 | 3.7 | 3.3 | 3.4 | 3.1 | 3.7 | E/ | 3.7 | 3.5 | 3.8 | | | | | | | | | | |
| 29607 | 3.3 | 3.3 | 3.4 | 3.7 | 3.4 | 3.6 | 3.6/ | 3.7 | 3.2 | 3.3 | 3.5 | 3.8 | 3.9 | 3.2 | 1.6 | 3.1 | 3.7 | 2.8 | 3.1 | | | | | | |
| 29611 | 3.6 | 4.0 | 3.2 | 3.7/ | | | | | | | | | | | | | | | | | | | | | |
| 29612 | 3.6 | 3.3 | 4.1/ | 3.3 | 3.5 | | | | | | | | | | | | | | | | | | | | |
| 29614 | 3.4 | 3.7 | 3.1 | 3.3 | E | 3.4 | E | 3.6 | 3.1 | 3.2 | 3.6/ | 3.1 | 3.4 | 3.2 | 3.7 | 3.6 | 3.6 | 3.0 | | | | | | | |
| 29620 | 3.5 | 3.2 | 3.6 | E | 3.4 | 3.6 | 3.5 | 3.6 | E/ | 3.7 | 3.6 | 3.5 | 3.5 | 3.5 | 3.8 | | | | | | | | | | |
| 29622 | 2.9 | 2.5 | 2.8 | 2.8 | 2.8 | 3.0 | 2.8 | 3.2/ | 2.9 | 3.1 | 2.9 | 3.1 | 3.0 | 3.0 | | | | | | | | | | | |
| 29625 | 3.3 | 3.3 | 3.5 | 3.2 | 3.3 | 3.4 | 3.4 | 3.4 | 3.5 | E/ | 3.5 | 3.1 | 3.1 | 3.0 | 3.4 | 3.0 | 3.4 | 3.5 | | | | | | | |
| 29629 | 3.5 | 3.8 | 3.3 | 3.5 | 3.3 | 3.6 | 3.4 | 3.6/ | 3.6 | E | 3.7 | E | 3.5 | 3.4 | 3.3 | 3.0 | | | | | | | | | |
| 29631 | 3.7 | 3.8 | 3.4 | 3.9 | 3.9 | 3.8 | 3.7 | 3.0 | 3.6 | E | 3.9/ | 3.9 | 3.9 | 3.8 | 3.8 | 3.5 | 3.5 | | | | | | | | |
| 29636 | 3.7 | 3.5 | 3.9 | 3.7/ | 3.8 | 3.6 | 3.3 | 3.7 | 3.9 | E | 3.4 | 3.7 | 3.7 | 3.7 | | | | | | | | | | | |
| 29637 | 3.5 | 3.3 | 3.8 | 3.6 | 3.6 | 3.6 | 3.4 | 3.5 | 3.6 | 2.9 | 3.9/ | 3.5 | 2.8 | 3.6 | 3.8 | 3.7 | E | 3.5 | 3.5 | 3.4 | 3.4 | | | | |
| 29648 | 3.9 | 3.9/ | 4.1 | 4.0 | 3.5 | 3.8 | 3.8 | 3.9 | | | | | | | | | | | | | | | | | |
| 29649 | 3.5 | 3.3 | 3.4 | 3.3 | 3.6 | 3.1 | 3.4 | 3.3 | 3.8 | 3.7/ | 3.7 | 3.6 | 3.5 | 3.6 | 3.7 | 3.9 | 3.4 | E | 3.2 | | | | | | |
| 29650 | 3.3 | 3.0 | 3.6 | 3.2 | 3.4 | 3.2 | 3.2 | 3.3 | 3.7/ | 3.3 | 3.1 | 3.2 | 3.3 | 3.3 | 3.4 | 3.2 | 3.0 | | | | | | | | |
| 29657 | 3.4 | 3.2 | 2.4 | 3.4 | 3.5 | 3.3 | 3.5 | 3.7/ | 3.5 | 3.3 | 3.5 | E | 3.7 | 2.9 | 3.7 | 3.4 | | | | | | | | | |
| 29664 | 3.5 | 3.4 | 3.4 | 3.5 | 3.6 | 3.8 | 3.4 | 3.6/ | 3.6 | 3.4 | 3.4 | 3.5 | 3.7 | 3.5 | 3.6 | 3.6 | | | | | | | | | |
| 29670 | 3.2 | 3.3 | 3.4 | E | 3.4 | 3.5 | 3.3 | 3.6/ | 3.4 | 3.2 | 2.7 | 3.0 | 3.1 | 3.2 | 3.4 | E | 3.3 | 3.3 | 2.8 | | | | | | |
| 29676 | 3.2 | 3.1 | 3.3 | 3.4 | 2.8 | 3.1 | 3.3 | 3.0 | 3.2 | 3.0 | 3.0/ | 3.6 | 3.0 | 3.1 | 3.4 | 3.5 | 3.5 | 3.6 | 2.8 | | | | | | |
| 29677 | 3.5 | 3.2 | 3.1 | 3.9 | 3.8 | 3.9 | E | 3.5/ | 3.5 | 3.5 | E | 3.4 | 3.6 | 3.8 | 3.6 | 3.6 | 3.8 | 3.0 | 2.0 | | | | | | |
| 29678 | 3.5 | 3.7 | 3.4 | 3.8 | 3.6 | 3.6 | 3.3 | 3.5/ | 3.4 | 3.5 | 3.6 | 3.7 | 3.5 | 3.8 | 3.6 | 3.5 | 3.1 | 3.5 | | | | | | | |
| 29688 | 3.5 | 3.4 | 3.6 | 3.5 | 3.7 | 3.5/ | 3.3 | 3.6 | 3.7 | 3.6 | 3.7 | 3.7 | 3.4 | E | 3.5 | 3.1 | 3.8 | 3.5 | | | | | | | |
| 29700 | 3.4 | 3.6 | 3.2 | 3.5 | 2.9 | 3.4 | 3.4 | 3.1 | 3.4 | 3.6/ | 3.7 | 3.3 | 3.4 | 3.4 | 3.5 | 3.1 | 3.8 | 3.5 | | | | | | | |

MEAN 3.5
 S.D. 0.21
 N 24

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

TABLE 27
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL WEIGHTS (GRAMS)

| FETUS # | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
|---------|-------------------------|---------|-----|-----|------|------|------|---------|------|------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| DAM # | GROUP 4: 1000 MG/KG/DAY | | | | | | | | | | | | | | | | | | | | | | |
| MEAN | 3.0 | E / 3.3 | 3.3 | 3.0 | 3.0 | 3.0 | 2.9 | E | 3.1 | 3.4 | 2.5 | 2.7 | 3.2 | 3.4 | 3.2 | 3.5 | 3.2 | 3.6 | 3.2 | 3.7 | 3.3 | 3.5 | |
| S.D. | 3.3 | 3.5 | E | 3.4 | 3.5 | 3.4 | 3.4 | 3.0 | 3.6 | E | 3.0/ | E | 3.2 | 3.4 | 3.4 | 3.7 | 3.5 | 3.7 | 3.4 | 3.4 | 3.7 | 3.1 | 3.1 |
| N | 3.5 | 3.6 | 3.7 | 3.4 | E | 3.8/ | 3.6 | 3.4 | 3.5 | E | 3.5 | 3.7 | E | 3.6 | 3.6 | 3.5 | 3.5 | 3.6 | 3.6 | 3.6 | 3.3 | 3.3 | 3.1 |
| | 3.3 | 2.7 | 3.2 | 3.4 | 3.1 | 3.3 | 3.6 | E / 2.9 | 3.4 | 3.3 | 3.5/ | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.3 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.1 |
| | 3.4 | 3.1 | 3.4 | 3.3 | 3.5 | 3.0 | 3.5 | 3.4 | 3.3 | 3.5/ | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.3 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.1 |
| | 2.8 | 2.5 | E | 2.4 | 2.7 | 2.8 | E | 2.6 | 2.8 | 2.7/ | 3.1 | 2.9 | 2.8 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.7 |
| | 3.7 | 3.6 | 4.0 | 3.8 | 3.6 | E | 3.7 | 3.7 | 3.8/ | 3.7 | 3.5 | 3.8 | 4.1 | 3.8 | 3.2 | 3.7 | 3.8 | 3.8 | 3.8 | 3.8 | 3.8 | 3.2 | 3.7 |
| | 3.2 | 3.1 | 3.1 | 3.6 | 3.4 | 3.2 | 3.5 | E / 3.4 | 3.2 | 3.2 | 3.1 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 |
| | 3.0 | 3.5 | 3.2 | 3.4 | 2.9 | 3.1/ | 2.9 | 3.0 | 3.0 | 3.0 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 |
| | 3.6 | 3.6 | E | 3.8 | 3.8 | 4.1 | 3.8/ | 3.6 | 3.8 | 3.6 | 3.9 | 3.8 | 3.2 | 3.3 | 3.6 | 3.2 | 3.3 | 3.6 | 3.2 | 3.3 | 3.6 | 3.2 | 3.2 |
| | 3.3 | 3.4 | 3.5 | 3.4 | 3.1 | 3.5 | 3.3 | E / | E | 3.3 | 3.1 | 3.4 | 3.1 | 3.1 | 3.3 | 3.2 | 3.3 | 3.6 | 3.2 | 3.1 | 3.3 | E | 3.3 |
| | 3.0 | 2.9 | 2.9 | 3.0 | 3.0 | 3.1 | 3.1 | 3.3 | 3.0/ | 2.8 | 3.0 | 2.6 | 3.4 | 3.3 | 2.9 | 2.8 | 3.3 | 2.9 | 2.8 | 3.3 | 2.9 | 2.8 | 2.8 |
| | 3.5 | 3.5 | 3.7 | 3.4 | 3.7 | 3.1 | 3.5 | 3.3 | 3.4/ | 3.2 | 3.6 | 3.4 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.7 | 3.5 |
| | 2.9 | 2.7 | 2.6 | 3.2 | 3.5 | 3.0/ | 3.6 | 3.0 | 2.9 | 3.0 | 3.4 | 2.8 | 3.5 | E | E | E | E | E | E | E | E | E | E |
| | 4.2 | / | 4.1 | 4.3 | | | | | | | | | | | | | | | | | | | |
| | 3.4 | 3.3 | 3.0 | 3.3 | 3.5 | 3.5 | 3.4 | 3.3/ | 3.1 | 3.8 | 3.3 | 3.7 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 | 3.3 |
| | 3.3 | 3.3 | 3.2 | 3.2 | 3.2/ | 3.0 | E | 3.7 | 3.5 | 3.2 | 3.6 | 3.0 | 3.3 | 2.9 | 3.4 | 3.4 | 3.4 | 3.4 | 3.4 | 3.4 | 3.4 | 3.4 | 3.4 |
| | 3.3 | 3.4 | 3.1 | 3.4 | 3.5 | 3.1 | 3.6 | 3.6/ | 3.3 | 3.4 | 3.2 | 3.4 | 3.3 | 3.5 | 3.4 | 3.2 | 3.5 | 3.4 | 3.2 | 3.5 | 3.4 | 3.2 | 3.1 |
| | 3.5 | E | 3.2 | 3.4 | 3.7 | 3.7 | 3.3 | 3.3/ | 3.7 | 3.2 | 3.6 | 3.2 | 3.6 | 3.3 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.6 | 3.4 |
| | 2.8 | 2.5 | 2.7 | 2.7 | L | 3.2 | 2.7 | 2.9 | 2.8 | 2.5/ | 2.9 | 2.8 | 3.0 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 2.9 | 3.4 |
| | 3.0 | 2.1 | 2.8 | 3.0 | 3.0 | 2.8 | 3.2 | 3.1/ | 3.3 | 3.2 | 3.3 | 3.2 | 3.0 | 2.7 | 3.0 | 3.1 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| | 3.4 | 3.2 | 3.5 | 3.2 | 3.5 | 3.4 | 3.6 | 3.3 | 3.5/ | 3.4 | 3.5 | 3.3 | 3.7 | 3.2 | 3.1 | 3.2 | 3.2 | 3.2 | 3.2 | 3.2 | 3.2 | 3.2 | 3.1 |

MEAN 3.3
S.D. 0.32
N 22

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

GRADE

DAMS FROM GROUP 1: 0 MG/KG/DAY FETUS #

29599

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
 A A A A A A E A A A A A A A A
 SEX: M M M M F M - M F F M M M M F

SKELETAL 5 V CERVICAL CENTRUM #1 OSSIFIED P
 EXTERNAL 7 EARLY RESORPTION P
 SKELETAL 9 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 12 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 13 V CERVICAL CENTRUM #1 OSSIFIED P
 VISCERAL 14 M HEART AND/OR GREAT VESSEL ANOMALY P
 TRANSPOSITION OF THE GREAT VESSELS; RIGHT CAROTID AND RIGHT
 SUBCLAVIAN ARISE INDEPENDENTLY FROM AORTIC ARCH (NO
 BRACHIOCEPHALIC TRUNK); LEFT CAROTID AND LEFT SUBCLAVIAN
 FORM COMMON VESSEL ARISING FROM AORTIC ARCH; INTERVENTRICULAR
 SEPTUM ABSENT

SKELETAL 15 V CERVICAL CENTRUM #1 OSSIFIED P
 NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,8,9,10,11,12,13,14,15
 1,2,3,4,5,6,8,9,10,11,12,13,15
 1,2,3,4,6,8,10,11,14

29601

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
 A A A E A A A A A A A A A A A A A A
 SEX: F M F - F M F F F M M M M M M M M M

EXTERNAL 4 EARLY RESORPTION P
 SKELETAL 7 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 10 V CERVICAL CENTRUM #1 OSSIFIED

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

PAGE 2

| DAMS FROM GROUP | 1: | 0 | MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------|----|-----------|--|-------|
| 29601 | (CONTINUED) | | | | |
| | EXTERNAL | | | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | | | 1,2,3,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20 | |
| | SKELETAL | | | 1,2,3,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20 | |
| 29602 | | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 | |
| | | | | A A A A A A A A A A A A A A A A | |
| | | | | SEX: F F F F M F F M M M F M F F M F M | |
| | SKELETAL | 1 | | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 3 | | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 4 | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 9 | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | | | #5 | |
| | | | | V REDUCED OSSIFICATION OF THE 13TH RIB(S) | 1 |
| | | | | RIGHT | |
| | SKELETAL | 10 | | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 12 | | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 16 | | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | | | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 | |
| | SKELETAL | | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 | |
| | | | | 2,5,6,7,8,11,13,14,15,17 | |
| 29609 | | | | 1 | |
| | | | | A/ | |
| | | | | SEX: M | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 1: 0 MG/KG/DAY | FETUS # | NO REMARKABLE OBSERVATIONS | GRADE | |
|-----------------|----------------|----------|--|--|---|
| 29609 | (CONTINUED) | EXTERNAL | 1 | | |
| | | VISCERAL | 1 | | |
| | | SKELETAL | 1 | | |
| 29615 | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 | | |
| | | | A A A A A A A A A A A A A | | |
| | | SEX: | F F M F M M F M F F F M | | |
| | | SKELETAL | 2 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | SKELETAL | 4 | #5 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | SKELETAL | 5 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | 1 |
| | | SKELETAL | 10 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | SKELETAL | 11 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| | | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13 | |
| | | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13 1,3,6,7,8,9,12,13 | |
| 29619 | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 | | |
| | | | A A A A A A A/E A A A A A E A A | | |
| | | SEX: | M F F F F F F - F F F M M - M M | | |
| | | SKELETAL | 1 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | SKELETAL | 3 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | SKELETAL | 5 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | SKELETAL | 7 | V CERVICAL CENTRUM #1 OSSIFIED | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 1: 0 MG/KG/DAY FETUS # GRADE

29628 (CONTINUED)

| | | | |
|----------|----|----------------------------------|---|
| SKELETAL | 3 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 4 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 5 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 6 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 7 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 8 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 10 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 12 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 13 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14 | |
| SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14 | |
| | | 1,2,9,11,14 | |

29634

| | | | | | | | | | | | | | | | |
|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| | A | A | A | A | A | A | A | A | A | A | A | A | A | A | A |
| SEX: | F | F | F | M | M | F | F | M | F | F | F | F | F | M | F |

29639

| | | | |
|----------|----|--|---|
| SKELETAL | 3 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | #5 | |
| SKELETAL | 4 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 6 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 7 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 11 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | |
| SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | |
| | | 1,2,5,8,9,10,12,13,14,15 | |

29639

| | | | | | | | | | | | | | | | |
|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| | A | A | E | A | A | A | A | A | A | A | E | A | A | A | A |
| SEX: | F | M | - | M | M | M | F | M | M | - | F | F | M | F | M |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

| DAMS FROM GROUP | 1: 0 MG/KG/DAY | FETUS # | GRADE |
|-----------------|----------------|--|-------|
| 29639 | (CONTINUED) | | |
| EXTERNAL | 3 | EARLY RESORPTION | 1 |
| SKELETAL | 4 | V BENT RIB(S) #11 AND #12, RIGHT | |
| SKELETAL | 6 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 7 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| SKELETAL | 8 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 9 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| EXTERNAL | 10 | EARLY RESORPTION | |
| SKELETAL | 11 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| SKELETAL | 12 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| VISCERAL | | 1,2,4,5,6,7,8,9,11,12,13,14,15 | |
| SKELETAL | | 1,2,4,5,6,7,8,9,11,12,13,14,15 1,2,5,13,14,15 | |
| | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | | E E A A A E/A A A E A A E A | |
| | | SEX: - - F M F - F F M - M F M - F | |
| 29640 | | | |
| EXTERNAL | 1 | EARLY RESORPTION | |
| EXTERNAL | 2 | EARLY RESORPTION | |
| EXTERNAL | 6 | EARLY RESORPTION | |
| EXTERNAL | 10 | EARLY RESORPTION | |
| SKELETAL | 13 | V 7TH CERVICAL RIB(S) | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 1: 0 MG/KG/DAY | FETUS # | | GRADE |
|-----------------|----------------|---------|--|-------|
| 29640 | (CONTINUED) | | | |
| | EXTERNAL | 14 | PINPOINT, RIGHT EARLY RESORPTION | |
| | SKELETAL | 15 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | 2 |
| | EXTERNAL | | V 25 PRESACRAL VERTEBRAE | P |
| | VISCERAL | | NO REMARKABLE OBSERVATIONS | |
| | SKELETAL | | 3,4,5,7,8,9,11,12,13,15 3,4,5,7,8,9,11,12,13,15 3,4,5,7,8,9,11,12 | |
| 29644 | | | 1 2 3 4 5 6 7 8 9 10 11 A/A A A A A A A E A A A SEX: M M M M M F M - F F F | |
| | SKELETAL | 2 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) LEFT | 1 |
| | SKELETAL | 6 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) LEFT | 1 |
| | EXTERNAL | 8 | EARLY RESORPTION | |
| | SKELETAL | 9 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | | | V 7TH CERVICAL RIB(S) | P |
| | SKELETAL | 10 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) PINPOINT, RIGHT BILATERAL | 1 |
| | | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 11 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) LEFT | 1 |
| | | | V 25 PRESACRAL VERTEBRAE | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

| DAMS FROM GROUP | 1: 0 MG/KG/DAY | FETUS # | GRADE |
|-----------------|----------------|--|-------|
| 29644 | (CONTINUED) | | |
| | SKELETAL | 11 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,9,10,11 | |
| | SKELETAL | 1,2,3,4,5,6,7,9,10,11 1,3,4,5,7 | |
| 29647 | | | |
| | SKELETAL | 1 2 3 4 5 6 7 8 9 10 11 12 13 | |
| | SKELETAL | A A A/A A A A A A A A A A | |
| | SKELETAL | SEX: F F F M M M F M F M M M | |
| | SKELETAL | 5 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 7 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 AND #6 | P |
| | SKELETAL | 9 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 1,2,3,4,6,8,10,11,12,13 | |
| 29652 | | | |
| | | 1 | |
| | | A/ | |
| | | SEX: F | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1 | |
| | SKELETAL | 1 | |
| | SKELETAL | 1 | |
| 29660 | | | |
| | EXTERNAL | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 | |
| | VISCERAL | A A A A A E A/A A A A A A A A | |
| | SKELETAL | SEX: M F M M M - M F M M M M F M M | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

| DAMS FROM GROUP | 1: 0 MG/KG/DAY | FETUS # | GRADE |
|-----------------|----------------|--|-------|
| 29662 | (CONTINUED) | | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,4,5,6,7,8,9,10,11,12,13,14,15 | |
| | SKELETAL | 1,4,5,6,7,8,9,10,11,12,13,14,15 | |
| | | 1,5,7,8,9,11,12,13,15 | |
| 29669 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | | A A A A A A E A/ A A A A A A E | |
| | | SEX: F M M F M - M F F M F M M - | |
| | SKELETAL | 3 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 4 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 7 EARLY RESORPTION | |
| | SKELETAL | 8 V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | 3 |
| | SKELETAL | 10 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | V REDUCED OSSIFICATION OF THE 13TH RIB(S) | 3 |
| | SKELETAL | 11 V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 2 |
| | | LEFT | |
| | SKELETAL | 12 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 14 V REDUCED OSSIFICATION OF THE 13TH RIB(S) LEFT | 2 |
| | EXTERNAL | 15 EARLY RESORPTION | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,8,9,10,11,12,13,14 | |
| | SKELETAL | 1,2,3,4,5,6,8,9,10,11,12,13,14 | |
| | | 1,2,5,6,9,13 | |
| 29674 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | | A A A A A A A E A A A/ A A A A | |
| | | SEX: F M F M M F M - F M M M M M M | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 1: 0 MC/KG/DAY FETUS # GRADE

29695 (CONTINUED)

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14
 1,2,3,4,5,6,7,8,9,10,11,12,13,14
 1,2,3,4,6,7,9,10,11,12,13,14
 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
 A E E A A A A A A A A A A A A A
 SEX: M - - F F M M F M F F F F F M

29696

EXTERNAL 2 EARLY RESORPTION
 EXTERNAL 3 EARLY RESORPTION
 SKELETAL 4 V CERVICAL CENTRUM #1 OSSIFIED
 SKELETAL 5 V CERVICAL CENTRUM #1 OSSIFIED
 SKELETAL 12 V CERVICAL CENTRUM #1 OSSIFIED
 SKELETAL 14 V CERVICAL CENTRUM #1 OSSIFIED
 NO REMARKABLE OBSERVATIONS
 1,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,6,7,8,9,10,11,13,15,16

P
 P
 P
 P

29709

1 2 3 4 5 6 7 8 9 10 11 12
 A A A A E A A A A A A A
 SEX: M F M F - M F F F F F F

EXTERNAL 5 EARLY RESORPTION
 SKELETAL 7 V REDUCED OSSIFICATION OF THE 13TH RIB(S)
 RIGHT

1

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
SPONSOR: VELSIOOL

TABLE 28
A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 1: 0 MG/KG/DAY FETUS #

GRADE

29709 (CONTINUED)

NO REMARKABLE OBSERVATIONS
EXTERNAL 1,2,3,4,6,7,8,9,10,11,12
VISCERAL 1,2,3,4,6,7,8,9,10,11,12
SKELETAL 1,2,3,4,6,8,9,10,11,12

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 2: 30 MG/KG/DAY FETUS # GRADE

29591
 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
 A A A A A A A/A A A A A A A A
 SEX: F F M F M M F M F F F F F F F

SKELETAL 3 V STERNEBRA(E) #5 AND/OR #6 UNOSSFIED P
 #5

SKELETAL 4 V STERNEBRA(E) #5 AND/OR #6 UNOSSFIED P
 #5

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15
 1,2,5,6,7,8,9,10,11,12,13,14,15

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
 A A A A A A/A A A A A A A A A A A A
 SEX: F F M F F M F M F F F F F F M F M F

SKELETAL 11 V CERVICAL CENTRUM #1 OSSIFIED P
 NO REMARKABLE OBSERVATIONS

EXTERNAL
 VISCERAL
 SKELETAL
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18
 1,2,3,4,5,6,7,8,9,10,12,13,14,15,16,17,18

29600
 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
 E A A A/A A A A A A A A A A A A A A
 SEX: - M M F M F F F F M F F M M M M M

EXTERNAL 1 EARLY RESORPTION
 SKELETAL 7 V STERNEBRA(E) #5 AND/OR #6 UNOSSFIED P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 2: 30 MG/KG/DAY FETUS # GRADE

 29600 (CONTINUED)

| | | | |
|----------|----|---|--------|
| SKELETAL | 8 | #5 AND #6 V STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED #4 | P |
| SKELETAL | 9 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 AND #6 | P |
| SKELETAL | 18 | V CERVICAL CENTRUM #1 OSSIFIED V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P P |
| EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| VISCERAL | | 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 | |
| SKELETAL | | 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 2, 3, 4, 5, 6, 10, 11, 12, 13, 14, 15, 16, 17 | |
| | | 1 2 3 4 5 6 7 8 9 10 A A A A A A A A A A SEX: F F F F F F F F F F | |
| SKELETAL | 2 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 5 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| VISCERAL | | 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 | |
| SKELETAL | | 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 1, 3, 4, 6, 7, 8, 9, 10 | |
| | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 A A A A A A A A A A A A A A A A SEX: F M M F F F F F F F F F F F F F F | |
| SKELETAL | 10 | V CERVICAL CENTRUM #1 OSSIFIED | P |

29605
 134

29606

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 2: 30 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-----------------|---------|---|
| 29606 | (CONTINUED) | | |
| | SKELETAL | 11 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16 |
| | | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16 |
| 29610 | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 |
| | | | A A A A/ A A A A A A A A A A |
| | | | SEX: F M M M M F M M M F F F F M M |
| | | | NO REMARKABLE OBSERVATIONS |
| | EXTERNAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| 29617 | | | 1 2 3 4 5 6 7 8 9 10 11 12 |
| | | | A A A/ E A A A E A A A A |
| | | | SEX: M F M - F M F - M F F M |
| | SKELETAL | 1 | V CERVICAL CENTRUM #1 OSSIFIED |
| | VISCERAL | 3 | V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, LEFT |
| | SKELETAL | | V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #3 AND #4 |
| | EXTERNAL | 4 | EARLY RESORPTION |
| | SKELETAL | 7 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | 8 | EARLY RESORPTION |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 2: 30 MG/KG/DAY FETUS # GRADE

29624 (CONTINUED)

EXTERNAL
 VISCERAL
 SKELETAL

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16
 5,6,8,9,10,11,12,13

29630

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
 A A A A A A A A A A A A A A A
 SEX: F F M M F F M F F F M M F M F F

SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL
 EXTERNAL
 VISCERAL
 SKELETAL

1 V REDUCED OSSIFICATION OF THE 13TH RIB(S)
 LEFT
 10 V CERVICAL CENTRUM #1 OSSIFIED
 11 V CERVICAL CENTRUM #1 OSSIFIED
 12 V CERVICAL CENTRUM #1 OSSIFIED
 14 V CERVICAL CENTRUM #1 OSSIFIED
 15 V CERVICAL CENTRUM #1 OSSIFIED
 NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15
 2,3,4,5,6,7,8,9,13

1
 P
 P
 P
 P
 P

29633

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
 A A A A A A A A A A A A A A A A
 SEX: F M M F F F F F F F F F F F F M

EXTERNAL
 VISCERAL
 SKELETAL

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16

29635

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
 A E A A A A A A A A A A A A A A
 SEX: M - F M M F F F F F F F F M M M M M

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 2: 30 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-----------------|---|-------|
| 29635 | (CONTINUED) | | |
| | EXTERNAL | 2 EARLY RESORPTION | |
| | SKELETAL | 4 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 7 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,3,4,5,6,7,8,9,10,11,12,13,14,15,16 | |
| | SKELETAL | 1,3,4,5,6,7,8,9,10,11,12,13,14,15,16 | |
| | | 1,3,5,6,8,9,10,11,12,13,14,15,16 | |
| 29642 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 | |
| | | A A A A A/ A A A A A A E A A | |
| | | SEX: M F F M M F F F F M F F - F F | |
| | SKELETAL | 1 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 6 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 12 EARLY RESORPTION | |
| | SKELETAL | 13 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,13,14 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,13,14 | |
| | | 2,3,4,5,7,8,9,10,11,14 | |
| 29646 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 | |
| | | A A A A A A/ A A A A A A A A A A A | |
| | | SEX: F M M F F F F F F M F F M F M F | |
| | SKELETAL | 1 V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| | SKELETAL | 3 V CERVICAL CENTRUM #1 OSSIFIED | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

DAMS FROM GROUP 2: 30 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 2: 30 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-----------------|---|-------|
| 29663 | (CONTINUED) | | |
| | SKELETAL | #5 V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| | SKELETAL | 10 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | #5 14 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | #5 V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| | | V 7TH CERVICAL RIB(S) PINPOINT, BILATERAL | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 1,2,4,6,7,11,12,13,15,16,17 | |
| 29666 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 A A A A A A A E E A A/A A SEX: M F M F F F M - - M M F M | |
| | SKELETAL | 1 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 2 M MICROPTHALMIA AND/OR ANOPHTHALMIA ANOPHTHALMIA, RIGHT | |
| | VISCERAL | M EXENCEPHALY WITH OR WITHOUT OPEN EYELID ABLEPHARIA, LEFT | P |
| | SKELETAL | CONFIRMATION OF EXENCEPHALY CONFIRMATION OF ANOPHTHALMIA V 14TH RUDIMENTARY RIB(S) BILATERAL | P |
| | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 2: 30 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-----------------|---------|--|
| 29667 | (CONTINUED) | | |
| | EXTERNAL | 11 | EARLY RESORPTION |
| | SKELETAL | 12 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 15 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 16 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,7,9,10,12,13,14,15,16 |
| | SKELETAL | | 1,2,3,4,5,7,9,10,12,13,14,15,16 |
| | | | 1,2,3,4,5,7,9,13,14 |
| 29668 | | 1 | 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 |
| | | | A A A A A A A A/A A A A A A A A A |
| | | | SEX: F M M M M M F M M F M M M M M M M |
| | SKELETAL | 2 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 5 | V CERVICAL CENTRUM #1 OSSIFIED |
| | | | V 14TH RUDIMENTARY RIB(S) |
| | | | RIGHT |
| | SKELETAL | 9 | V 14TH FULL RIB(S) |
| | | | BILATERAL |
| | SKELETAL | 17 | V 14TH RUDIMENTARY RIB(S) |
| | | | BILATERAL |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 |
| | | | 1,3,4,6,7,8,10,11,12,13,14,15,16,18 |
| 29673 | | 1 | 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 |
| | | | A A A A A A A A/A A A A A A A A A |
| | | | SEX: F F M M M F F M M M M M M F M |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL

GRADE

| DAMS FROM GROUP | 2: 30 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-----------------|--|-------|
| 29673 | (CONTINUED) | | |
| | SKELETAL | 1 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 3 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 6 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 7 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 9 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 11 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 13 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 15 M FILAMENTOUS TAIL 8 MM IN LENGTH | P |
| | VISCERAL | CONFIRMATION OF FILAMENTOUS TAIL | P |
| | SKELETAL | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | V 25 PRESACRAL VERTEBRAE | P |
| | | CONFIRMATION OF FILAMENTOUS TAIL | P |
| | | ALL VERTEBRAE POSTERIOR TO LUMBAR #5 ABSENT; LUMBAR ARCH #5 LOCATED MORE MEDIAL THAN NORMAL, BILATERAL; LUMBAR CENTRUM #5 ABSENT | |
| | | NO REMARKABLE OBSERVATIONS | |
| | EXTERNAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,16 | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,16 | |
| | SKELETAL | 2,4,5,8,10,12,14,16 | |
| 29675 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 | |
| | | A A A A A A A A A A A A A | |
| | | SEX: F M F F F F F F M M F F M F | |
| | SKELETAL | 8 V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 2 |
| | SKELETAL | 10 V REDUCED OSSIFICATION OF THE 13TH RIB(S) | 1 |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 2: | 30 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------|---|-------------------------------------|-------|
| 29675 | (CONTINUED) | | | |
| | | | 11 | P |
| | SKELETAL | | | |
| | | RIGHT | | |
| | | V REDUCED OSSIFICATION OF THE 13TH RIB(S) | | |
| | | MODERATE, RIGHT; SLIGHT, LEFT | | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 | | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 | | |
| | | 1,2,3,4,5,6,7,9,12,13 | | |
| 29685 | | | | |
| | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | | | A A A A A A A A A A A A A A A A | |
| | | SEX: M F M F M F M F M F M F M F M | | |
| | SKELETAL | | 3 | P |
| | | V CERVICAL CENTRUM #1 OSSIFIED | | |
| | | V 7TH CERVICAL RIB(S) | | |
| | SKELETAL | PINPOINT, RIGHT | 5 | P |
| | | V BENT RIB(S) | | |
| | | #11 AND #12, RIGHT | | |
| | SKELETAL | | 7 | P |
| | | V CERVICAL CENTRUM #1 OSSIFIED | | |
| | SKELETAL | | 8 | P |
| | | V CERVICAL CENTRUM #1 OSSIFIED | | |
| | SKELETAL | | 9 | P |
| | | V CERVICAL CENTRUM #1 OSSIFIED | | |
| | | V BENT RIB(S) | | |
| | | #7 THROUGH #10, RIGHT | | |
| | SKELETAL | | 11 | P |
| | | V CERVICAL CENTRUM #1 OSSIFIED | | |
| | SKELETAL | | 13 | P |
| | | V CERVICAL CENTRUM #1 OSSIFIED | | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | | |
| | | 1,2,4,6,10,12,14,15 | | |
| 29698 | | | | |
| | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 | |
| | | | A A A A A A A A A A A A A A | |
| | | SEX: F F M F M F F M M M F F M | | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 2: 30 MG/KG/DAY FETUS # GRADE

29698 (CONTINUED) SKELETAL 12 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 P

NO REMARKABLE OBSERVATIONS

EXTERNAL 1,2,3,4,5,6,7,8,9,10,11,12,13
 VISCERAL 1,2,3,4,5,6,7,8,9,10,11,12,13
 SKELETAL 1,2,3,4,5,6,7,8,9,10,11,13

29710 1 2 3 4 5 6 7 8 9 10 11 12 13 14
 A A A A A A A A A A A A A A A
 SEX: M F F M F F F F F F F F F M M M M

SKELETAL 3 V 7TH CERVICAL RIB(S) P

PINPOINT, LEFT

SKELETAL 4 V CERVICAL CENTRUM #1 OSSIFIED P
 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 P

SKELETAL 5 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 13 V CERVICAL CENTRUM #1 OSSIFIED P

NO REMARKABLE OBSERVATIONS

EXTERNAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14
 VISCERAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14
 SKELETAL 1,2,6,7,8,9,10,11,12,14

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|---|-------|
| 29592 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 A A A A A A A A/A A A E A A A A SEX: M M F M M M F M M F M - F F F M | |
| | SKELETAL | 1 V 14TH RUDIMENTARY RIB(S) LEFT | P |
| | SKELETAL | 2 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 4 V 14TH RUDIMENTARY RIB(S) LEFT | P |
| | SKELETAL | 7 V 14TH RUDIMENTARY RIB(S) RIGHT | P |
| | SKELETAL | 10 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 11 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 12 EARLY RESORPTION | P |
| | SKELETAL | 13 V CERVICAL CENTRUM #1 OSSIFIED V 14TH RUDIMENTARY RIB(S) LEFT | P |
| | SKELETAL | 14 V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #3 AND #4 | 1 |
| | SKELETAL | 16 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,13,14,15,16 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,13,14,15,16 3,5,6,8,9,15 | |
| 29596 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 A A A A A A A A A A E/A A A SEX: F M F F F F F F F F - M F M | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|---------|--|
| 29596 | (CONTINUED) | | |
| | SKELETAL | 2 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 6 | V CERVICAL CENTRUM #1 OSSIFIED |
| | | | V 14TH RUDIMENTARY RIB(S) |
| | EXTERNAL | 12 | RIGHT EARLY RESORPTION |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,13,14,15 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,13,14,15 |
| | | | 1,3,4,5,7,8,9,10,11,13,14,15 |
| 29607 | | | |
| | SKELETAL | 14 | V STERNEBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED |
| | SKELETAL | 18 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 |
| | | | 1,2,3,4,5,6,7,8,9,10,11,12,13,15,16,17 |
| 29611 | | | |
| | | 1 | 2 |
| | | A | A A/ |
| | | SEX: | M M F |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 PROJECT NO.: WIL-15218 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSICOL INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|--|-------|
| 29611 | (CONTINUED) | | |
| | EXTERNAL | | |
| | VISCERAL | | |
| | SKELETAL | | |
| | | NO REMARKABLE OBSERVATIONS | |
| | | 1,2,3 | |
| | | 1,2,3 | |
| | | 1,2,3 | |
| 29612 | | 1 2 3 4 | |
| | | A A/ A A | |
| | | SEX: M M F M | |
| | SKELETAL | 3 V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| | | NO REMARKABLE OBSERVATIONS | |
| | EXTERNAL | 1,2,3,4 | |
| | VISCERAL | 1,2,3,4 | |
| | SKELETAL | 1,2,4 | |
| 29614 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 | |
| | | A A A E A A A A/ A A A A A A A A A | |
| | | SEX: M F F - M - M F F F F F F M F M M | |
| | SKELETAL | 2 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 4 EARLY RESORPTION | P |
| | SKELETAL | 5 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 6 EARLY RESORPTION | P |
| | SKELETAL | 7 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 11 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 15 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 16 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 17 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 18 V CERVICAL CENTRUM #1 OSSIFIED | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS # GRADE

29614 (CONTINUED)

EXTERNAL
 VISCERAL
 SKELETAL

NO REMARKABLE OBSERVATIONS
 1,2,3,5,7,8,9,10,11,12,13,14,15,16,17,18
 1,2,3,5,7,8,9,10,11,12,13,14,15,16,17,18
 1,3,8,9,10,12,13,14

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
 A A E A A A E/ A A A A A A A A
 SEX: F F - F F F M - F F F F F F M

29620

SKELETAL
 SKELETAL
 EXTERNAL
 SKELETAL
 SKELETAL
 EXTERNAL
 SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL
 EXTERNAL
 VISCERAL
 SKELETAL

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
 V 7TH CERVICAL RIB(S)
 PINPOINT, RIGHT
 V CERVICAL CENTRUM #1 OSSIFIED
 3 EARLY RESORPTION
 5 V CERVICAL CENTRUM #1 OSSIFIED
 6 V CERVICAL CENTRUM #1 OSSIFIED
 8 EARLY RESORPTION
 9 V CERVICAL CENTRUM #1 OSSIFIED
 10 V CERVICAL CENTRUM #1 OSSIFIED
 12 V CERVICAL CENTRUM #1 OSSIFIED
 13 V CERVICAL CENTRUM #1 OSSIFIED
 14 V CERVICAL CENTRUM #1 OSSIFIED
 15 V CERVICAL CENTRUM #1 OSSIFIED
 NO REMARKABLE OBSERVATIONS
 1,2,4,5,6,7,9,10,11,12,13,14,15
 1,2,4,5,6,7,9,10,11,12,13,14,15
 4,7,11

P P P P P P P P P P

29622

1 2 3 4 5 6 7 8 9 10 11 12 13 14
 A A A A E A A A/ A A A A A A A
 SEX: F M F M - F M M M F F M M F

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---|-------|
| 29622 | (CONTINUED) | | |
| | SKELETAL | 1 V STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED #2 | P |
| | EXTERNAL SKELETAL | 5 EARLY RESORPTION | |
| | SKELETAL | 8 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,6,7,8,9,10,11,12,13,14 | |
| | SKELETAL | 1,2,3,4,6,7,8,9,10,11,12,13,14 2,3,4,6,7,9,10,11,12,13,14 | |
| 29625 | SKELETAL | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 A A A A A A A A E/ A A A A A A A SEX: M M M M M M M M - M M F F M F M M | 1 |
| | EXTERNAL SKELETAL | 7 V REDUCED OSSIFICATION OF THE 13TH RIB(S) LEFT | |
| | SKELETAL | 10 EARLY RESORPTION | |
| | SKELETAL | 15 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 16 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | V CERVICAL CENTRUM #1 OSSIFIED | |
| | VISCERAL | NO REMARKABLE OBSERVATIONS | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,11,12,13,14,15,16,17,18 1,2,3,4,5,6,7,8,9,11,12,13,14,15,16,17,18 1,2,3,4,5,6,8,9,11,12,13,14,17,18 | |
| 29629 | SKELETAL | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 A A A A A A A/ A E A E A A A SEX: M F F F M M M F - M - F F M F | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|---------|---|
| 29629 | (CONTINUED) | | |
| EXTERNAL | | 9 | EARLY RESORPTION |
| EXTERNAL | | 11 | EARLY RESORPTION |
| SKELETAL | | 13 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 |
| VISCERAL | | 14 | V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) KIDNEY (W/O AND HOAR GRADE 0), LEFT; URETER, SLIGHT, LEFT |
| EXTERNAL | | | NO REMARKABLE OBSERVATIONS |
| VISCERAL | | | 1,2,3,4,5,6,7,8,10,12,13,14,15 |
| SKELETAL | | | 1,2,3,4,5,6,7,8,10,12,13,15 |
| | | | 1,2,3,4,5,6,7,8,10,12,14,15 |
| | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 |
| | | | A A A A A A A A E A/A A A A A |
| | | | SEX: F F M M M M F M - M F M F M M M |
| SKELETAL | | 1 | V CERVICAL CENTRUM #1 OSSIFIED |
| SKELETAL | | 5 | V CERVICAL CENTRUM #1 OSSIFIED |
| SKELETAL | | 8 | V CERVICAL CENTRUM #1 OSSIFIED |
| EXTERNAL | | 9 | EARLY RESORPTION |
| SKELETAL | | 10 | V CERVICAL CENTRUM #1 OSSIFIED |
| SKELETAL | | 11 | V CERVICAL CENTRUM #1 OSSIFIED |
| SKELETAL | | 13 | V 14TH RUDIMENTARY RIB(S) BILATERAL |
| SKELETAL | | 14 | V CERVICAL CENTRUM #1 OSSIFIED |
| SKELETAL | | 16 | V CERVICAL CENTRUM #1 OSSIFIED |
| EXTERNAL | | | NO REMARKABLE OBSERVATIONS |
| VISCERAL | | | 1,2,3,4,5,6,7,8,10,11,12,13,14,15,16 |
| SKELETAL | | | 1,2,3,4,5,6,7,8,10,11,12,13,14,15,16 |
| | | | 2,3,4,6,7,12,15 |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

29631

PROJECT NO.: WIL-15218
 SPONSOR: VELSCOOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|---------|---|
| 29636 | EXTERNAL | 9 | EARLY RESORPTION |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| | | | 1,2,3,4,5,6,7,8,10,11,12,13 |
| 29637 | SKELETAL | 12 | V 14TH RUDIMENTARY RIB(S) LEFT |
| | SKELETAL | 15 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | 16 | EARLY RESORPTION |
| | SKELETAL | 18 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 20 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,17,18,19,20 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,17,18,19,20 |
| | | | 1,2,3,4,5,6,7,8,9,10,11,13,14,17,19 |
| | | | 1,2,3,4,5,6,7 |
| 29648 | | | A/A A A A A A |
| | | | SEX: F M M F F M F |
| | | | 1 2 3 4 5 6 7 |
| | | | A/A A A A A A |
| | | | SEX: F M M F F M F |
| | | | 1 2 3 4 5 6 7 |
| | | | A/A A A A A A |
| | | | SEX: F M M F F M F |
| | | | 1 2 3 4 5 6 7 |
| | | | A/A A A A A A |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|--|-------|
| 29648 | (CONTINUED) | | |
| | EXTERNAL | | |
| | VISCERAL | | |
| | SKELETAL | | |
| | | NO REMARKABLE OBSERVATIONS | |
| | | 1,2,3,4,5,6,7 | |
| | | 1,2,3,4,5,6,7 | |
| | | 1,2,3,4,5,6,7 | |
| 29649 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 | |
| | | A A A A A A A A/A A A A A A A A A | |
| | | SEX: M F M M M F M F F F F M M M F - F | |
| | SKELETAL | 2 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 4 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 5 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 7 V 7TH CERVICAL RIB(S) PINPOINT, RIGHT | P |
| | SKELETAL | 10 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 11 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 13 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 14 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | EXTERNAL | 17 EARLY RESORPTION | |
| | SKELETAL | 18 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS # GRADE

 29649 (CONTINUED)

EXTERNAL
 VISCERAL
 SKELETAL

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,18
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,18
 1,3,6,8,9,12,15,16

29650

| | | | | | | | | | | | | | | | | | |
|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | |
| | A | A | A | A | A | A | A | A | A | A | A | A | A | A | A | A | A |
| SEX: | F | M | F | M | F | F | M | F | F | M | F | F | M | F | F | M | F |

| | | | | | | | | | | | | | | | | | |
|----------|----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|---|
| SKELETAL | 2 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | P |
| | | V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | | | | | | | | | | | | | | | 1 |
| SKELETAL | 3 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | P |
| SKELETAL | 4 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | P |
| SKELETAL | 5 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | P |
| SKELETAL | 6 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | | | | | | | | | | | | | | | 1 |
| | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | | | | | | | | | | | | | | | P |
| SKELETAL | 7 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | | | | | | | | | | | | | | | 3 |
| SKELETAL | 8 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | P |
| | | V 7TH CERVICAL RIB(S) INTERMEDIATE, LEFT | | | | | | | | | | | | | | | P |
| | | V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | | | | | | | | | | | | | | | 3 |
| SKELETAL | 9 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | P |
| SKELETAL | 10 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | | | | | | | | | | | | | | | 2 |
| | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | | | | | | | | | | | | | | | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSFOOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

PAGE 37

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | | GRADE |
|-----------------|------------------|---------|---|-------|
| 29650 | (CONTINUED) | | | |
| | | 12 | #5 V REDUCED OSSIFICATION OF THE 13TH RIB(S) LEFT | 3 |
| | | 13 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 3 |
| | | 15 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | | V REDUCED OSSIFICATION OF THE 13TH RIB(S) BILATERAL | 3 |
| | | | NO REMARKABLE OBSERVATIONS | |
| | | | EXTERNAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16 | |
| | | | VISCERAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16 | |
| | | | SKELETAL 1,11,14,16 | |
| 1 | 29657 | | | |
| 55 | | | | |
| | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | | | A A A A A A/A A A A A A A A | |
| | | | SEX: M F M F F M F F F F F F F M | |
| | | 3 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | 4 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | | #5 | |
| | | 6 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | | | #5 | |
| | | 7 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | 11 | EARLY RESORPTION | |
| | | 12 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) RIGHT | 1 |
| | | 14 | V REDUCED OSSIFICATION OF THE 13TH RIB(S) | 1 |
| | | | LEFT | |
| | | | V BENT RIB(S) #11, RIGHT | 1 |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 3: 300 MG/KG/DAY | FETUS # | GRADE |
|-----------------|------------------|--|-------|
| 29657 | (CONTINUED) | | |
| | EXTERNAL | | |
| | VISCERAL | | |
| | SKELETAL | | |
| | | NO REMARKABLE OBSERVATIONS | |
| | | 1,2,3,4,5,6,7,8,9,10,12,13,14,15 | |
| | | 1,2,3,4,5,6,7,8,9,10,12,13,14,15 | |
| | | 1,2,5,8,9,10,13,15 | |
| 29664 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | | A A A A A A/A A A A A A A A | |
| | | SEX: F M F M M F F F F M F M M M | |
| | | NO REMARKABLE OBSERVATIONS | |
| | EXTERNAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 | |
| 29670 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 | |
| | | A A E A A A A/A A A A A A A E A A A | |
| | | SEX: M M - M M F M M F F M F F F F F | |
| | | NO REMARKABLE OBSERVATIONS | |
| | EXTERNAL | 3 EARLY RESORPTION | |
| | SKELETAL | 7 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 11 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | 15 EARLY RESORPTION | |
| | SKELETAL | 16 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | NO REMARKABLE OBSERVATIONS | |
| | EXTERNAL | 1,2,4,5,6,7,8,9,10,11,12,13,14,16,17,18 | |
| | VISCERAL | 1,2,4,5,6,7,8,9,10,11,12,13,14,16,17,18 | |
| | SKELETAL | 1,2,4,5,6,8,9,10,12,13,14,17,18 | |
| 29676 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 | |
| | | A A A A A A A A A/A A A A A A A A A | |
| | | SEX: M M F M F F M F M F M M M M M F | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS #

GRADE

29678

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
 A A A A A A/A A A A A A A A A A A
 SEX: F F M M F F F F F F F F M M M M M M M

SKELETAL 2 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 P

SKELETAL 4 V CERVICAL CENTRUM #1 OSSIFIED P

SKELETAL 5 V CERVICAL CENTRUM #1 OSSIFIED P

SKELETAL 8 V 14TH RUDIMENTARY RIB(S) BILATERAL P

SKELETAL 9 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 P

SKELETAL 13 V CERVICAL CENTRUM #1 OSSIFIED P

SKELETAL 15 V CERVICAL CENTRUM #1 OSSIFIED P

SKELETAL 15 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 P

NO REMARKABLE OBSERVATIONS

EXTERNAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17
 VISCERAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17
 SKELETAL 1,3,6,7,10,11,12,14,16,17

29688

1 2 3 4 5 6 7 8 9 10 11 12 13 14
 A A A A/A A A A A A A A A A E
 SEX: M M M M M F M M F M F M M -

EXTERNAL 14 EARLY RESORPTION

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DEVOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL
 TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 3: 300 MG/KG/DAY FETUS # GRADE
 29688 (CONTINUED)

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13
 1,2,3,4,5,6,7,8,9,10,11,12,13
 1,2,3,4,5,6,7,8,9,10,11,12,13

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
 A A A A A A A A A A A A A A A A
 SEX: M F F F F M F M F M F F F M F M F

29700

SKELETAL 10 V CERVICAL CENTRUM #1 OSSIFIED
 NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17
 1,2,3,4,5,6,7,8,9,11,12,13,14,15,16,17

P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

29597

| EXTERNAL SKELETAL | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | GRADE |
|-------------------|----|---|---|---|---|---|---|---|---|----|----|----|-------|
| | | E/ | A | A | A | A | E | A | E | A | A | A | |
| | | SEX: - | F | M | M | M | - | F | - | F | F | F | |
| EXTERNAL SKELETAL | 1 | EARLY RESORPTION | | | | | | | | | | | P |
| | 4 | V 14TH RUDIMENTARY RIB(S) LEFT | | | | | | | | | | | |
| EXTERNAL | 6 | EARLY RESORPTION | | | | | | | | | | | |
| EXTERNAL | 8 | EARLY RESORPTION | | | | | | | | | | | |
| SKELETAL | 10 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | |
| SKELETAL | 11 | V 14TH RUDIMENTARY RIB(S) BILATERAL | | | | | | | | | | | |
| | 12 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | | | | | | | | | | | P |
| SKELETAL | 12 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | | | | | | | | | | | P |

NO REMARKABLE OBSERVATIONS

2,3,4,5,7,9,10,11,12
 2,3,4,5,7,9,10,11,12
 2,3,5,7,9

29598

| EXTERNAL SKELETAL | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | GRADE |
|-------------------|----|--------------------------------|---|---|---|---|---|---|---|----|-----|----|----|----|----|----|-------|
| | | A | A | E | A | A | A | A | A | E | A/E | A | A | A | A | A | |
| | | SEX: F | M | - | F | F | M | M | M | M | - | M | - | M | F | F | |
| EXTERNAL SKELETAL | 3 | EARLY RESORPTION | | | | | | | | | | | | | | | P |
| SKELETAL | 5 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | |
| SKELETAL | 7 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | |
| EXTERNAL | 10 | EARLY RESORPTION | | | | | | | | | | | | | | | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE | | | | | | | | | | | | | | | | | |
|-----------------|------------------------------------|---------|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|--|--|--|
| 29598 | (CONTINUED) | 12 | EARLY RESORPTION | | | | | | | | | | | | | | | | | |
| | | 14 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | | | |
| | | | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | | | | | | | | | | | | | | | | | |
| | | | #5 | | | | | | | | | | | | | | | | | |
| | | 16 | V CERVICAL CENTRUM #1 OSSIFIED | | | | | | | | | | | | | | | | | |
| | | | NO REMARKABLE OBSERVATIONS | | | | | | | | | | | | | | | | | |
| | | | 1,2,4,5,6,7,8,9,11,13,14,15,16 | | | | | | | | | | | | | | | | | |
| | | | 1,2,4,5,6,7,8,9,11,13,14,15,16 | | | | | | | | | | | | | | | | | |
| | | | 1,2,4,6,8,9,11,13,15 | | | | | | | | | | | | | | | | | |
| | | | SEX: M M M M - M F M M - M M F | | | | | | | | | | | | | | | | | |
| 29608 | | 3 | V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) | | | | | | | | | | | | | | | | | |
| | | | #4 | | | | | | | | | | | | | | | | | |
| | | 4 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | | | | | | | | | | | | | | | | | |
| | | | #5 | | | | | | | | | | | | | | | | | |
| | | 5 | EARLY RESORPTION | | | | | | | | | | | | | | | | | |
| | | 8 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | | | | | | | | | | | | | | | | | |
| | | | #5 | | | | | | | | | | | | | | | | | |
| | | 10 | EARLY RESORPTION | | | | | | | | | | | | | | | | | |
| | | 13 | EARLY RESORPTION | | | | | | | | | | | | | | | | | |
| | | 16 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | | | | | | | | | | | | | | | | | |
| | #5 | | | | | | | | | | | | | | | | | | | |
| | NO REMARKABLE OBSERVATIONS | | | | | | | | | | | | | | | | | | | |
| | 1,2,3,4,6,7,8,9,11,12,14,15,16 | | | | | | | | | | | | | | | | | | | |
| | 1,2,3,4,6,7,8,9,11,12,14,15,16 | | | | | | | | | | | | | | | | | | | |
| | 1,2,6,7,9,11,12,14,15 | | | | | | | | | | | | | | | | | | | |
| | SEX: F F M M F M M - F M M M F F F | | | | | | | | | | | | | | | | | | | |
| 29613 | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | | | |
| | | | | | | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | | | | | | | | | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---------|--|
| 29613 | (CONTINUED) | | |
| | EXTERNAL SKELETAL | 8 | EARLY RESORPTION |
| | | 9 | V 7TH CERVICAL RIB(S) INTERMEDIATE, BILATERAL NO REMARKABLE OBSERVATIONS |
| | EXTERNAL SKELETAL | | 1,2,3,4,5,6,7,9,10,11,12,13,14,15,16 |
| | VISCERAL SKELETAL | | 1,2,3,4,5,6,7,9,10,11,12,13,14,15,16 |
| | | | 1,2,3,4,5,6,7,10,11,12,13,14,15,16 |
| 29616 | | | |
| | EXTERNAL SKELETAL | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 |
| | VISCERAL SKELETAL | | A A A A A A A A A A A A A A A A |
| | | | SEX: F F F M M F M M F M F M F M M |
| | | | NO REMARKABLE OBSERVATIONS |
| | EXTERNAL SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| | VISCERAL SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| | | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| 29618 | | | |
| | EXTERNAL SKELETAL | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 |
| | VISCERAL SKELETAL | | A E A A A E A A A A A A A A A A A A |
| | | | SEX: F - F M M - F M M M F F M M F M M |
| | | | NO REMARKABLE OBSERVATIONS |
| | EXTERNAL SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 |
| | VISCERAL SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15 |
| | | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 |
| 29621 | | | |
| | EXTERNAL SKELETAL | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 |
| | VISCERAL SKELETAL | | A A A A E A A A A A A A A A A A A |
| | | | SEX: M M M F - F F M F M F M F F F |
| | | | NO REMARKABLE OBSERVATIONS |
| | EXTERNAL SKELETAL | | 1,3,4,5,7,8,9,10,11,12,13,14,15,16,17 |
| | VISCERAL SKELETAL | | 1,3,4,5,7,8,9,10,11,12,13,14,15,16,17 |
| | | | 1,3,4,5,8,9,10,11,12,13,14,15,16,17 |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---------|---|
| 29621 | (CONTINUED) | | |
| | SKELETAL | 3 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 4 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 |
| | EXTERNAL | 5 | EARLY RESORPTION |
| | SKELETAL | 6 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 7 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 |
| | SKELETAL | 12 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 13 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 14 | V CERVICAL CENTRUM #1 OSSIFIED |
| | SKELETAL | 15 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,6,7,8,9,10,11,12,13,14,15,16 |
| | SKELETAL | | 1,2,3,4,6,7,8,9,10,11,12,13,14,15,16 |
| | | | 1,2,8,9,10,11,16 |
| | | | 1 2 3 4 5 6 7 8 9 10 11 12 13 |
| | | | A A A A A A E/ A A A A A A |
| | | | SEX: M F M M F F - F F F F F M |
| | SKELETAL | 1 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 |
| | | | V BENT RIB(S) |
| | | | #11, BILATERAL |
| | SKELETAL | 2 | V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 |
| | SKELETAL | 6 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | 7 | EARLY RESORPTION |
| 29626 | | | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 SPONSOR: VELSICOL

INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---|-------|
| 29626 | (CONTINUED) | | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,8,9,10,11,12,13 | |
| | SKELETAL | 1,2,3,4,5,6,8,9,10,11,12,13 3,4,5,8,9,10,11,12,13 | |
| 29632 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 A A A A A A A A A A A A A SEX: M F M F M F M F M F M F M F | |
| | VISCERAL | 3 RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) RIGHT | P |
| | SKELETAL | 4 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | P |
| | SKELETAL | 7 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 9 V CERVICAL CENTRUM #1 OSSIFIED V 7TH CERVICAL RIB(S) | P |
| | SKELETAL | 11 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED PINPOINT, LEFT #5 | P |
| | SKELETAL | 12 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 | |
| | SKELETAL | 1,2,4,5,6,7,8,9,10,11,12,13 1,2,3,5,6,8,10,13 | |
| 29638 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 A E A A A A A A A A A A A A A SEX: F - M M M M M M M M M M M M M F | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-------------------|-------------------|--|-------|
| 29638 | (CONTINUED) | | |
| EXTERNAL SKELETAL | 2 | EARLY RESORPTION | P |
| SKELETAL | 3 | V 14TH RUDIMENTARY RIB(S) LEFT | P |
| SKELETAL | 5 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 10 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 11 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| | | V 14TH RUDIMENTARY RIB(S) BILATERAL | P |
| SKELETAL | 12 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 13 | V CERVICAL CENTRUM #1 OSSIFIED | P |
| SKELETAL | 14 | V 14TH RUDIMENTARY RIB(S) RIGHT | P |
| EXTERNAL | | NO REMARKABLE OBSERVATIONS | |
| VISCERAL | | 1,3,4,5,6,7,8,9,10,11,12,13,14,15,16 | |
| SKELETAL | | 1,3,4,5,6,7,8,9,10,11,12,13,14,15,16 | |
| | | 1,4,6,7,8,9,15,16 | |
| | 29641 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 | |
| | | A A A A A A E/E E A A A A A A A | |
| | | SEX: M F M M M F - - M M M F F M - F M | |
| VISCERAL | 4 | M SITUS INVERSUS TRACHEA, ESOPHAGUS, GREAT AND MAJOR VESSELS, LIVER, STOMACH, HEART, LUNGS, SPLEEN, INTESTINE AND PANCREAS Laterally TRANSPOSED | P |
| EXTERNAL | 7 | EARLY RESORPTION | |
| EXTERNAL | 8 | EARLY RESORPTION | |
| EXTERNAL | 9 | EARLY RESORPTION | |
| SKELETAL | 10 | V 14TH RUDIMENTARY RIB(S) LEFT | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---|-------|
| 29641 | (CONTINUED) | | |
| | SKELETAL | 12 V 14TH RUDIMENTARY RIB(S) BILATERAL | P |
| | EXTERNAL | 16 EARLY RESORPTION | |
| | SKELETAL | 17 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,10,11,12,13,14,15,17,18 | |
| | SKELETAL | 1,2,3,4,5,6,10,11,12,13,14,15,17,18 1,2,3,4,5,6,11,13,14,15,18 | |
| 29643 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 A A A A A A A A A A A A A A A A SEX: F M M F F M F M F M F M M F M F | |
| | SKELETAL | 2 V 14TH RUDIMENTARY RIB(S) LEFT | P |
| | SKELETAL | 5 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 9 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 12 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 16 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 1,3,4,6,7,8,10,11,13,14,15,17,18 | |
| 29651 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 A A A A A A A A A A A A A A A A SEX: M M M M M F M F M F M M M M M | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---------|--|
| 29651 | (CONTINUED) | | |
| | SKELETAL | 8 | V CERVICAL CENTRUM #1 OSSIFIED |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18 |
| 29655 | | | |
| | SKELETAL | 7 | V BENT RIB(S) |
| | EXTERNAL | 13 | #10 AND #11, LEFT |
| | EXTERNAL | 14 | EARLY RESORPTION |
| | EXTERNAL | 15 | EARLY RESORPTION |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2,3,4,5,6,7,8,9,10,11,12 |
| | SKELETAL | | 1,2,3,4,5,6,7,8,9,10,11,12 |
| 29659 | | | |
| | EXTERNAL | | 1 2 |
| | VISCERAL | | / A A |
| | SKELETAL | | SEX: M M |
| | EXTERNAL | | NO REMARKABLE OBSERVATIONS |
| | VISCERAL | | 1,2 |
| | SKELETAL | | 1,2 |
| 29665 | | | |
| | EXTERNAL | | 1 2 3 4 5 6 7 8 9 10 11 12 13 |
| | VISCERAL | | A A A A A A A/ A A A A |
| | SKELETAL | | SEX: F M F M F M F M M M F |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|--|--------|
| 29665 | (CONTINUED) | | |
| | SKELETAL | 2 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | SKELETAL | 5 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 6 V BENT RIB(S) #12, BILATERAL | 1 |
| | SKELETAL | 9 V BENT RIB(S) #4 THROUGH #6 AND #9 THROUGH #12, LEFT; #4 THROUGH #7, #9, #10 AND #12, RIGHT | 1 |
| | SKELETAL | 10 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | SKELETAL | 12 V BENT RIB(S) #6 AND #8 THROUGH #13, RIGHT; #11 AND #12, LEFT | 1 |
| | SKELETAL | 13 V CERVICAL CENTRUM #1 OSSIFIED | P |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 | |
| | SKELETAL | 1,2,3,4,5,6,7,8,9,10,11,12,13 1,3,4,7,8,11 | |
| 29671 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 A A A A A/A E A A A A A A A A SEX: F F F F F F F - M M F M M M F M | |
| | SKELETAL | 2 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED #5 | P |
| | EXTERNAL | 7 EARLY RESORPTION | |
| | SKELETAL | 8 V CERVICAL CENTRUM #1 OSSIFIED V 14TH RUDIMENTARY RIB(S) LEFT | P P |
| | VISCERAL | 9 V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, BILATERAL | 1 |
| | SKELETAL | 14 V CERVICAL CENTRUM #1 OSSIFIED | P |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSICOL

TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS #

29671 (CONTINUED)

EXTERNAL
 VISCERAL
 SKELETAL

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,8,9,10,11,12,13,14,15
 1,2,3,4,5,6,8,10,11,12,13,14,15
 1,3,4,5,6,9,10,11,12,13,15

29679

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
 A A A A A A A/A A A A A A A A A
 SEX: M F F F F M F F F F F M F M M F

SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL
 SKELETAL

7 V CERVICAL CENTRUM #1 OSSIFIED
 9 V 14TH RUDIMENTARY RIB(S)
 LEFT
 13 V REDUCED OSSIFICATION OF THE 13TH RIB(S)
 LEFT
 15 V 7TH CERVICAL RIB(S)
 PINPOINT, RIGHT
 16 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED
 #5

P
 P
 1
 P
 P

29680

EXTERNAL
 VISCERAL
 SKELETAL

NO REMARKABLE OBSERVATIONS
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16
 1,2,3,4,5,6,8,10,11,12,14

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
 E A A A A A A/A A A A A A A A A
 SEX: - F M F M F M F M F F F F F M F

EXTERNAL
 SKELETAL

1 EARLY RESORPTION
 11 V CERVICAL CENTRUM #1 OSSIFIED

P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PROJECT NO.: WIL-15218
 SPONSOR: VELSIOOL
 TABLE 28
 A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS
 INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS

| DAMS FROM GROUP | 4: 1000 MG/KG/DAY | FETUS # | GRADE |
|-----------------|-------------------|---|-------|
| 29680 | (CONTINUED) | | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 | |
| | SKELETAL | 2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17 | |
| 29682 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 | |
| | EXTERNAL | A A A L A A A A A A A A A A A A | |
| | | SEX: F M M - M F M M F M M F F M M | |
| | EXTERNAL | LATE RESORPTION | |
| | | CROWN-RUMP LENGTH: 1.7 CM, MUMMIFIED | |
| | EXTERNAL | NO REMARKABLE OBSERVATIONS | |
| | VISCERAL | 1,2,3,5,6,7,8,9,10,11,12,13,14,15 | |
| | SKELETAL | 1,2,3,5,6,7,8,9,10,11,12,13,14,15 | |
| 29694 | | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 | |
| | SKELETAL | A A A A A A A A A A A A A A A A | |
| | | SEX: F F F M F M F M M M F M F F M M | |
| | SKELETAL | 1 V STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSFIED | P |
| | | #2 THROUGH #4 | |
| | SKELETAL | V STERNEBRA(E) #5 AND/OR #6 UNOSSFIED | P |
| | | #5 | |
| | SKELETAL | V STERNEBRA(E) #5 AND/OR #6 UNOSSFIED | P |
| | | #5 | |
| | SKELETAL | V 7TH CERVICAL RIB(S) | P |
| | | INTERMEDIATE, RIGHT | |
| | SKELETAL | V STERNEBRA(E) #5 AND/OR #6 UNOSSFIED | P |
| | | #5 AND #6 | |

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

DAMS FROM GROUP 4: 1000 MG/KG/DAY FETUS # GRADE

29694 (CONTINUED)

EXTERNAL NO REMARKABLE OBSERVATIONS
 VISCERAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17
 SKELETAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17
 5,6,7,8,9,10,11,12,13,14,15,16,17

29704
 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
 A A A A A A A A/ A A A A A A A
 SEX: M M F M M M F F M M M M M F F

SKELETAL 2 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 4 V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED P

SKELETAL 6 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 7 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 14 V CERVICAL CENTRUM #1 OSSIFIED P
 SKELETAL 15 V CERVICAL CENTRUM #1 OSSIFIED P

EXTERNAL NO REMARKABLE OBSERVATIONS
 VISCERAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15
 SKELETAL 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15
 1,3,5,8,9,10,11,12,13

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
 OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
 SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

WIL-15218
Velsicol Chemical Corporation

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

APPENDIX A

Analysis of Dosing Preparations (WIL Research Laboratories, Inc.)

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Analysis of Dosing Preparations

SUMMARY

The test material, isodecyl benzoate, exhibited a linear response with concentration by gas chromatography/flame ionization detection (FID) with splitless injection. The linear concentration range was 36.48 $\mu\text{g/ml}$ to 608 $\mu\text{g/ml}$.

In the range-finding study (WIL-15217), representative dosing preparations in corn oil at 25 mg/kg (5 mg/ml) and 1000 mg/kg (200 mg/ml) were analyzed to determine homogeneity and eight-day refrigerated stability. The preparations were found to be both homogeneous and stable.

The dosing preparations used in this study were analyzed on three occasions. The mean analyzed concentrations were between 97.3% and 107% of the target dose concentrations.

EXPERIMENTAL

Gas Chromatography

| | |
|-----------------------|---|
| Instrument: | Hewlett Packard 5890 Series II gas chromatograph with a 7673 autosampler and a 3396A integrator |
| Column: | J & W Scientific DB-5, 15-meter Megabore column with a 1.5 micron film thickness |
| Carrier: | Helium at 10 psig |
| Column Temperature: | 160°C for 0.5 min., ramp at 10°C/min. to 195°C and hold for 3 min., ramp at 20°C/min. to 290°C. |
| Detector: | FID at 290°C |
| Injector Temperature: | 250°C |
| Injector Volume: | 1 microliter, splitless |
| Retention Time: | Peak summation between 2.1 minutes and 4.5 minutes |

Standards

A primary standard was prepared by weighing approximately 25 to 35 milligrams of test material, isodecyl benzoate, into a tared glass weigh funnel and quantitatively transferring the

material to a 50-ml volumetric flask via a series of n-heptane washes and bringing to volume with n-heptane. Additional standards were prepared by diluting aliquots from this primary standard to give solutions with concentrations from approximately 50 to 105 $\mu\text{g/ml}$.

Samples

Samples of the dosing preparations were received from Pharmacy in scintillation vials. These were placed on a stir plate and stirred continuously while aliquots were withdrawn. The aliquots were withdrawn with a 1 cc tuberculin syringe, transferred to volumetric flasks and brought to volume with n-heptane. For all analyses, duplicate dilutions were prepared from all groups, except the control. Duplicate injections were made for each dilution and standard, with the dilutions being prepared so as to be bracketed by the standards.

Quantitation and Calibration

The isodecyl benzoate test material is not a single compound, but consists of over 20 isomers and related compounds. Rather than choosing a single peak for quantitation, the chromatographic peak areas were summed by the integrator and reported as a single peak. This summed peak area was then used for all further calculations. Figure 1 is a representative standard chromatogram.

For each set of analyses, a calibration curve was constructed using a spreadsheet least squares linear regression program (Microsoft Excel) using full floating decimal point calculations. The concentration of each dilution was calculated from the calibration curve; the concentrations of the dosing preparations were calculated by multiplying the dilution concentration by any necessary conversion factors. Concentration data were transferred to another Excel spreadsheet template; the percent concentration and statistics were calculated by the spreadsheet and presented in tabular form. Rounding may result in slightly different values if the calculations are repeated using the displayed data.

RESULTS

Linearity

Table I presents linearity data for a set of standards in the range of 36.48 to 608 $\mu\text{g/ml}$. The data demonstrated a linear response in this concentration range, with a mean concentration/area of $2.79 \text{ E-}04 \pm 7.7 \text{ E-}06$ (RSD = 2.7%).

Dosing Preparation Analyses

Prior to the start of the range-finding study (WIL-15217), representative corn oil formulations were prepared and analyzed for homogeneity and stability. The formulations were designated as Group 1 (5 mg/ml) and Group 2 (200 mg/ml). Table II presents the homogeneity data for the formulations prepared on 6/27/94. The data are summarized in Table III. The mean concentrations for Group 1 were 4.80 mg/ml (top, 95.9%), 4.91 mg/ml (mid, 98.2%) and 4.94 mg/ml (bottom, 98.8%). The overall mean was 4.88 mg/ml (97.6% of the target dose concentration). The mean concentrations for Group 2 were 201 mg/ml (top, 101%), 201 mg/ml (mid, 101%) and 200 mg/ml (bottom, 100%). The overall mean concentration was 201 mg/ml, or 100% of the dose concentration. All groups met with WIL SOP No. AC-086 requirements for homogeneity, i.e., the group mean differed by less than 15% from the target dose concentration for that group and the location means for each group differed by less than 10% from the overall mean for that group.

Samples collected on 6-27-94 from Groups 1 and 2 were stored refrigerated and analyzed on 7-5-94 for stability. The results are presented in Table IV. The mean concentration values for Group 1 top and bottom were 4.93 and 4.98 mg/ml, respectively (103% and 101% of the dose concentration). For Group 2, the values were 206 mg/ml (top, 102%) and 205 mg/ml (bottom, 103%). The preparations showed no apparent degradation and met WIL SOP No. AC-086 criteria for stability.

Three sets of dosing formulations were analyzed for the definitive study. The formulations were prepared and analyzed on 8-26-94, 9-2-94 and 9-9-94. The results are presented in Tables V through VIII and summarized in Table IX.

The data from the analyses of the 8-26-94 are presented in Tables V and VI. The results of the original analysis (Table V) showed concentrations that were within SOP limits of acceptability, but the data sets contained considerable scatter. The scatter was attributed to signal resulting from carry-out of corn oil components from one injection to the next. To alleviate this problem, a second temperature program was added to the GC column program to clear the column of corn oil components before the next injection. The same dilutions were analyzed using this modified program. The results (Table VI) showed improved precision. The modified program was used for the remaining analyses in this study. The use of the modified program did not adversely affect the validity of the method.

Table IX is a summary of the results of the analyses of the three sets of formulations. The mean concentrations were 6.11 mg/ml (Group 2, 102%), 61.0 mg/ml (Group 3, 102%) and 205 mg/ml (Group 4, 103%). All formulations met the WIL SOP No. AC-086 requirement for suspension concentration, i.e. within $\pm 15\%$ of the target dose concentration.

CONCLUSION

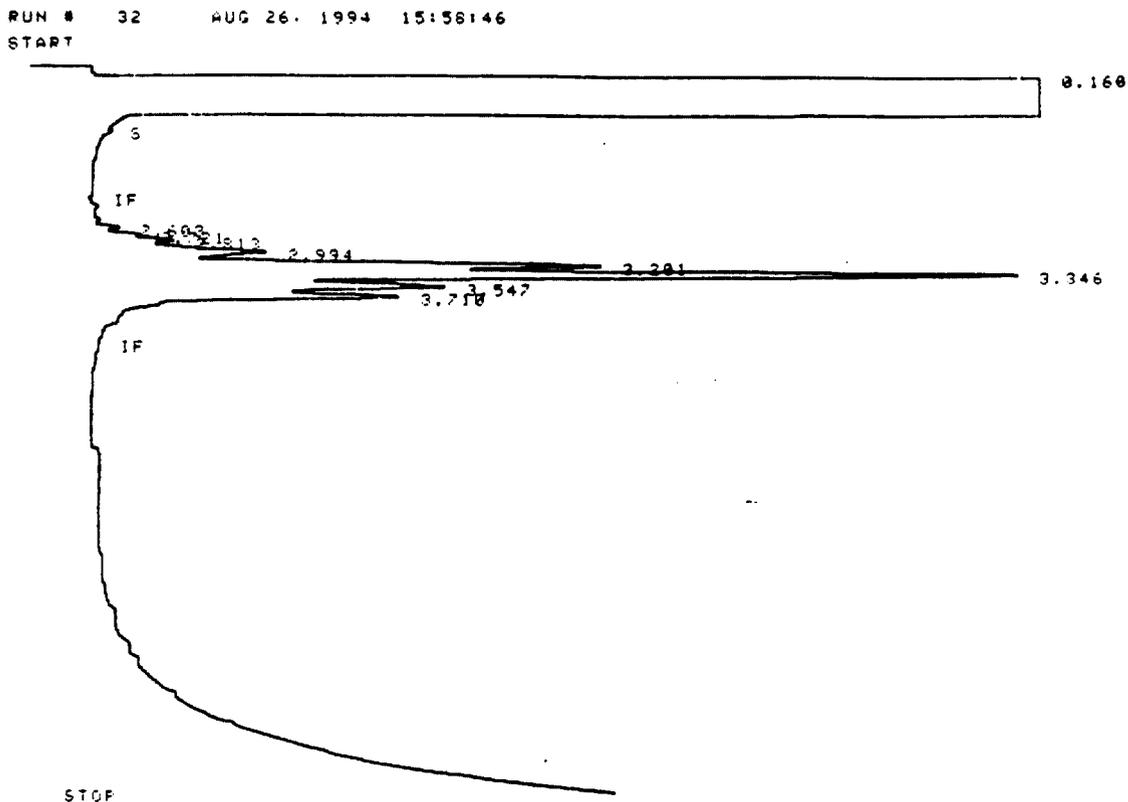
The representative corn oil formulations of isodecyl benzoate in WIL-15217 were homogeneous and stable for eight days when refrigerated.

The dosing formulations in the present study contained the amounts of the test material specified in the protocol.



Loren W. Severs, M.S.
Manager of Analytical Chemistry

Feb 10, 1995
Date



RUN# 32 AUG 26. 1994 15:58:46
 SAMPLE NAME: S-4 SAMPLE# 3

15218

| AREA# | RT | AREA | TYPE | WIDTH | AREA% |
|-------|-------|-----------|------|-------|----------|
| | .160 | 2.092E+09 | SBB | .026 | 99.98563 |
| | 3.300 | 381061 | ++ | .127 | .01439 |

Figure 1. Chromatogram of an Iodecyl Benzoate Standard

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table I: Linearity/Reproducibility Analysis - Second Run

Reference: WIL-15219, Vol. A-1, Pages 16-17

| Concentration (µg/ml) | Ref # | Run # | Area | Mean Area | SD | RSD (%) | Concentration/Mean Area (Response Factor) |
|--------------------------|-------|-------|---------|-----------|---------|---------|--|
| 36.48 | 16-2 | 183 | 107946 | 123845 | 8375 | 5.2 | 2.95E-04 |
| | | 184 | 125330 | | | | |
| | | 185 | 127129 | | | | |
| | | 186 | 128445 | | | | |
| | | 187 | 125694 | | | | |
| | | 188 | 125906 | | | | |
| | | 189 | 125321 | | | | |
| | | 190 | 125391 | | | | |
| 72.96 | 16-3 | 191 | 270812 | 264562 | 8604 | 3.3 | 2.76E-04 |
| | | 192 | 271168 | | | | |
| | | 193 | 256969 | | | | |
| | | 194 | 257553 | | | | |
| | | 195 | 256887 | | | | |
| | | 196 | 256027 | | | | |
| | | 197 | 273323 | | | | |
| | | 198 | 274756 | | | | |
| 121.6 | 16-4 | 199 | 435585 | 432637 | 12395 | 2.9 | 2.81E-04 |
| | | 200 | 425011 | | | | |
| | | 201 | 447658 | | | | |
| | | 202 | 423910 | | | | |
| | | 203 | 423841 | | | | |
| | | 204 | 422724 | | | | |
| | | 205 | 455059 | | | | |
| | | 206 | 427305 | | | | |
| 212.8 | 16-5 | 207 | 804912 | 774994 | 24018 | 3.1 | 2.75E-04 |
| | | 208 | 762971 | | | | |
| | | 209 | 751084 | | | | |
| | | 210 | 808967 | | | | |
| | | 211 | 744788 | | | | |
| | | 212 | 788729 | | | | |
| | | 213 | 776491 | | | | |
| | | 214 | 762027 | | | | |
| 334.4 | 16-6 | 215 | 1217975 | 1221218 | 23498 | 1.9 | 2.74E-04 |
| | | 216 | 1222297 | | | | |
| | | 217 | 1217238 | | | | |
| | | 218 | 1191958 | | | | |
| | | 219 | 1186246 | | | | |
| | | 220 | 1241899 | | | | |
| | | 221 | 1252987 | | | | |
| | | 222 | 1239166 | | | | |
| 425.6 | 16-7 | 223 | 1567980 | 1544871 | 20853 | 1.3 | 2.76E-04 |
| | | 224 | 1528676 | | | | |
| | | 225 | 1638055 | | | | |
| | | 226 | 1522853 | | | | |
| | | 227 | 1564159 | | | | |
| | | 228 | 1531283 | | | | |
| | | 229 | 1574775 | | | | |
| | | 230 | 1531589 | | | | |
| 608 | 16-1 | 231 | 2189398 | 2216580 | 38883 | 1.7 | 2.74E-04 |
| | | 232 | 2197544 | | | | |
| | | 233 | 2245027 | | | | |
| | | 234 | 2195787 | | | | |
| | | 235 | 2154854 | | | | |
| | | 236 | 2270878 | | | | |
| | | 237 | 2251547 | | | | |
| | | 238 | 2227805 | | | | |
| | | | | | | | |
| | | | | | Mean | | 2.79E-04 |
| | | | | | SD | | 7.7E-06 |
| | | | | | RSD (%) | | 2.7 |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table II: **Homogeneity Analysis of the 6-27-94 Preparations**
 (Performed 6-27-94)

Reference: Study WIL-15217, Vol. A-1, Pages 1-8

| Group # | Dose Conc (mg/ml) | Reference # (15217-) | Run # | Analyzed Concentration (mg/ml) | Percent of Target (%) | Mean Conc (mg/ml) | SD | RSD (%) | Mean Conc % of Target (%) |
|---------|----------------------|-------------------------|-------|-----------------------------------|--------------------------|----------------------|------|------------|------------------------------|
| 1 Top | 5.00 | 4- 1 | 7 | 4.81 | 96.2 | 4.80 | 0.16 | 3.3 | 95.9 |
| | | | 8 | 4.71 | 94.2 | | | | |
| | | | 9 | 5.01 | 100 | | | | |
| | | | 10 | 4.85 | 93.0 | | | | |
| 1 Mid | 5.00 | 4- 3 | 11 | 4.82 | 96.4 | 4.91 | 0.22 | 4.5 | 98.2 |
| | | | 12 | 4.93 | 98.6 | | | | |
| | | | 13 | 5.20 | 104 | | | | |
| | | | 14 | 4.68 | 93.6 | | | | |
| 1 Btm | 5.00 | 4- 5 | 15 | 4.76 | 95.2 | 4.94 | 0.25 | 5.0 | 98.8 |
| | | | 16 | 4.95 | 99.0 | | | | |
| | | | 17 | 4.76 | 95.2 | | | | |
| | | | 18 | 5.28 | 106 | | | | |
| 2 Top | 200 | 4- 13 | 19 | 198 | 99.0 | 201 | 6.3 | 3.1 | 101 |
| | | | 20 | 206 | 103 | | | | |
| | | | 21 | 194 | 97.0 | | | | |
| | | | 22 | 207 | 104 | | | | |
| 2 Mid | 200 | 4- 15 | 23 | 198 | 99.0 | 201 | 7.0 | 3.5 | 101 |
| | | | 24 | 208 | 104 | | | | |
| | | | 25 | 194 | 97.0 | | | | |
| | | | 26 | 201 | 101 | | | | |
| 2 Btm | 200 | 4- 17 | 27 | 202 | 101 | 200 | 1.7 | 0.85 | 100 |
| | | | 28 | 198 | 99.0 | | | | |
| | | | 29 | 201 | 101 | | | | |
| | | | 30 | 200 | 100 | | | | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table III: **Summary of Homogeneity/Concentration Means**
Homogeneity Analysis of the 6-27-94 Preparations

| Group | 1 | 2 |
|---------------------------|-------------|------------|
| Dose Conc (mg/ml) | 5.00 | 200 |
| Top | 4.80 | 201 |
| Mid | 4.91 | 201 |
| Btm | 4.94 | 200 |
| Group Mean (mg/ml) | 4.88 | 201 |
| SD | 0.075 | 0.52 |
| RSD% | 1.5 | 0.26 |
| Mean % of Target | 97.6 | 100 |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table IV: **Eight-Day Stability Analysis of the 6-27-94 Preparations**
 (Performed 7-5-94)

Reference: Study WIL-15217, Vol. A-1, pages 3,6-10

| Group # | Dose Conc (mg/ml) | Reference # (15217) | Run # | Analyzed Concentration (mg/ml) | Percent of Target (%) | Mean Conc (mg/ml) | SD | RSD (%) | Mean Conc % of Target (%) | Percent of Day Zero (%) |
|---------|----------------------|------------------------|-------|-----------------------------------|--------------------------|----------------------|------|------------|------------------------------|----------------------------|
| 1 Top | 5.00 | 7-1 | 43 | 4.97 | 99.4 | 4.93 | 0.17 | 3.4 | 98.7 | 103 |
| | | | 44 | 4.85 | 97.0 | | | | | |
| | | 7-2 | 45 | 5.15 | 103 | | | | | |
| | | | 46 | 4.76 | 95.2 | | | | | |
| 1 Btm | 5.00 | 7-3 | 47 | 5.15 | 103 | 4.98 | 0.13 | 2.6 | 99.5 | 101 |
| | | | 48 | 4.84 | 96.8 | | | | | |
| | | 7-4 | 49 | 4.96 | 99.2 | | | | | |
| | | | 50 | 4.95 | 99.0 | | | | | |
| 2 Top | 200 | 7-9 | 51 | 208 | 104 | 206 | 2.7 | 1.3 | 103 | 102 |
| | | | 52 | 207 | 104 | | | | | |
| | | 7-10 | 53 | 202 | 101 | | | | | |
| | | | 54 | 207 | 104 | | | | | |
| 2 Btm | 200 | 7-11 | 55 | 201 | 101 | 205 | 3.4 | 1.6 | 103 | 103 |
| | | | 56 | 204 | 102 | | | | | |
| | | 7-12 | 57 | 209 | 105 | | | | | |
| | | | 58 | 206 | 103 | | | | | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table V : Concentration Analysis of the 8-26-94 Preparations
(Performed 8-26-94)

Reference: Study WIL-15218 , Vol. A-1, Pages 1-6

| Group # | Dose Conc (mg/ml) | Reference # (15218-1) | Run # | Analyzed Concentration (mg/ml) | Percent of Target (%) | Mean Conc (mg/ml) | SD | RSD (%) | Mean Conc % of Target (%) |
|---------|----------------------|--------------------------|-------|-----------------------------------|--------------------------|----------------------|------|------------|------------------------------|
| 1 | 0.00 | 4- 1 | 7 , 8 | ----- Not Detected ----- | | | | | |
| 2 | 6.00 | 4- 2 | 9 | 6.42 | 107 | 6.62 | 0.30 | 4.5 | 110 |
| | | | 10 | 6.85 | 114 | | | | |
| | | 4- 3 | 11 | 6.31 | 105 | | | | |
| | | | 12 | 6.89 | 115 | | | | |
| 3 | 60.0 | 4- 8 | 13 | 62.4 | 104 | 65.0 | 5.4 | 8.3 | 108 |
| | | | 14 | 73.0 | 122 | | | | |
| | | 4- 9 | 15 | 62.7 | 104 | | | | |
| | | | 16 | 61.7 | 103 | | | | |
| 4 | 200 | 4- 10 | 17 | 184 | 92.0 | 203 | 13 | 6.2 | 101 |
| | | | 18 | 206 | 103 | | | | |
| | | 4- 11 | 19 | 210 | 105 | | | | |
| | | | 20 | 211 | 105 | | | | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table VI : Concentration Analysis of the 8-26-94 Preparations
(Performed 8-26-94)

Reference: Study WIL-15218 , Vol. A-1, Pages 1-6

| Group # | Dose Conc (mg/ml) | Reference # (15218-) | Run # | Analyzed Concentration (mg/ml) | Percent of Target (%) | Mean Conc (mg/ml) | SD | RSD (%) | Mean Conc % of Target (%) |
|---------|-------------------|----------------------|---------|--------------------------------|-----------------------|-------------------|-------|---------|---------------------------|
| 1 | 0.00 | 4- 1 | 33 , 34 | ----- Not Detected ----- | | | | | |
| 2 | 6.00 | 4- 2 | 35 | 6.49 | 108 | 6.44 | 0.063 | 0.97 | 107 |
| | | | 36 | 6.50 | 108 | | | | |
| | | 4- 3 | 37 | 6.38 | 106 | | | | |
| | | | 38 | 6.40 | 107 | | | | |
| 3 | 60.0 | 4- 8 | 39 | 63.1 | 105 | 63.8 | 2.9 | 4.6 | 106 |
| | | | 40 | 68.2 | 114 | | | | |
| | | 4- 9 | 41 | 62.6 | 104 | | | | |
| | | | 42 | 61.6 | 103 | | | | |
| 4 | 200 | 4- 10 | 43 | 205 | 102 | 208 | 2.9 | 1.4 | 104 |
| | | | 44 | 206 | 103 | | | | |
| | | 4- 11 | 45 | 210 | 105 | | | | |
| | | | 46 | 211 | 105 | | | | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table VII : Concentration Analysis of the 9-2-94 Preparations
(Performed 9-2-94)

Reference: Study WIL-15218 , Vol. A-1, Pages 10-14

| Group # | Dose Conc (mg/ml) | Reference # (15218-) | Run # | Analyzed Concentration (mg/ml) | Percent of Target (%) | Mean Conc (mg/ml) | SD | RSD (%) | Mean Conc % of Target (%) |
|---------|----------------------|-------------------------|---------|-----------------------------------|--------------------------|----------------------|-------|------------|------------------------------|
| 1 | 0.00 | 12- 1 | 59 , 60 | ----- Not Detected ----- | | | | | |
| 2 | 6.00 | 12- 2 | 61 | 5.85 | 97.6 | 5.84 | 0.034 | 0.59 | 97.3 |
| | | | 62 | 5.88 | 98.0 | | | | |
| | | 12- 3 | 63 | 5.83 | 97.2 | | | | |
| | | | 64 | 5.80 | 96.6 | | | | |
| 3 | 60.0 | 12- 8 | 65 | 58.1 | 96.8 | 58.7 | 1.5 | 2.5 | 97.8 |
| | | | 66 | 58.3 | 97.2 | | | | |
| | | 12- 9 | 67 | 60.8 | 101 | | | | |
| | | | 68 | 57.5 | 95.9 | | | | |
| 4 | 200 | 12- 10 | 69 | 200 | 100 | 199 | 2.7 | 1.4 | 99.6 |
| | | | 70 | 199 | 99.5 | | | | |
| | | 12- 11 | 71 | 202 | 101 | | | | |
| | | | 72 | 196 | 97.8 | | | | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table VIII : Concentration Analysis of the 9-9-94 Preparations
 (Performed 9-9-94)

Reference: Study WIL-15218 , Vol. A-1, Pages 15-19

| Group # | Dose Conc (mg/ml) | Reference # (15218-) | Run # | Analyzed Concentration (mg/ml) | Percent of Target (%) | Mean Conc (mg/ml) | SD | RSD (%) | Mean Conc % of Target (%) |
|---------|-------------------|----------------------|---------|--------------------------------|-----------------------|-------------------|------|---------|---------------------------|
| 1 | 0.00 | 17- 1 | 85 , 86 | ----- Not Detected ----- | | | | | |
| 2 | 6.00 | 17- 2 | 87 | 5.82 | 96.9 | 6.04 | 0.19 | 3.2 | 101 |
| | | | 88 | 6.12 | 102 | | | | |
| | | 17- 3 | 89 | 6.26 | 104 | | | | |
| | | | 90 | 5.95 | 99.2 | | | | |
| 3 | 60.0 | 17- 8 | 91 | 63.2 | 105 | 60.4 | 2.3 | 3.8 | 101 |
| | | | 92 | 57.7 | 96.2 | | | | |
| | | 17- 9 | 93 | 59.7 | 99.5 | | | | |
| | | | 94 | 60.9 | 101 | | | | |
| 4 | 200 | 17- 10 | 95 | 198 | 99.1 | 208 | 6.6 | 3.2 | 104 |
| | | | 96 | 211 | 105 | | | | |
| | | 17- 11 | 97 | 212 | 106 | | | | |
| | | | 98 | 211 | 106 | | | | |

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

Table IX : Summary of Concentration Means

| Dose Group | 2 | 3 | 4 |
|----------------------|------|------|-----|
| Dose Conc (mg/ml) | 6.00 | 60.0 | 200 |
| Prep Date | | | |
| 8/26/94 | 6.44 | 63.8 | 208 |
| 9/2/94 | 5.84 | 58.7 | 199 |
| 9/9/94 | 6.04 | 60.4 | 208 |
| Overall Mean (mg/ml) | 6.11 | 61.0 | 205 |
| SD | 0.31 | 2.6 | 5.2 |
| RSD (%) | 5.0 | 4.3 | 2.5 |
| Percent of Dose Conc | 102 | 102 | 103 |

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

APPENDIX B

WIL Historical Control Data (Sprague-Dawley CrI:CD®BR Rats) - Summary

STANDARD DEVIATION

| | | | |
|--|-------------|---------------|------|
| NO. OF STUDIES IN HISTORICAL CONTROL | 108 | | |
| NO. OF ANIMALS IN HISTORICAL CONTROL | 2677 | | |
| NO. OF ANIMALS THAT DIED | 1 | | |
| NO. OF ANIMALS THAT ABORTED/DELIVERED | 0 | | |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION | 2676 | | |
| NO. NONGRAVID | 265 | | |
| NO. GRAVID | 2411 | | |
| NO. OF DAMS WITH ONLY RESORPTIONS | 8 | | |
| NO. OF DAMS WITH LIVE FETUSES | 2403 | | |
| NO. OF FETUSES IN HISTORICAL CONTROL | 34139 | | |
| MEAN NO. OF VIABLE FETUSES/DAM | 14.2 | (10.7 - 16.5) | 0.94 |
| MEAN NO. OF POSTIMPLANTATION LOSS/DAM | 0.8 | (0.3 - 1.4) | 0.22 |
| % POSTIMPLANTATION LOSS/DAM [PERCENT PER LITTER] | 5.5 | (2.2 - 13.5) | |
| % EARLY RESORPTIONS/DAM [PERCENT PER LITTER] | 5.3 | (1.8 - 13.5) | |
| % LATE RESORPTIONS/DAM [PERCENT PER LITTER] | 0.1 | (0.0 - 3.2) | |
| % DEAD FETUSES/DAM [PERCENT PER LITTER] | 0.0a | (0.0 - 0.3) | |
| → MEAN NO. OF IMPLANTATIONS/DAM | 15.0 | (11.5 - 17.4) | 0.97 |
| ∞ MEAN NO. OF CORPORA LUTEA/DAM | 16.6 | (14.4 - 19.2) | 0.98 |
| ∞ FETAL SEX RATIO: MALE:FEMALE | 16847:17292 | | |
| % MALE | 49.3 | (41.6 - 56.7) | |
| % FEMALE | 50.7 | (43.3 - 58.4) | |
| MEAN FETAL BODY WEIGHT | 3.5 | (3.3 - 3.8) | 0.12 |

RANGE OF STUDY DATES

03/29/82 - 09/13/92

a = INCLUDES ONE DEAD FETUS THAT DOES NOT TABULATE DUE TO ROUNDING
() = RANGE

TOTAL NUMBER OF LITTERS EXAMINED 2403

TOTAL NUMBER OF FETUSES EXAMINED EXTERNALLY 34139
TOTAL NUMBER OF FETUSES EXAMINED VISCERALLY 23712
TOTAL NUMBER OF FETUSES EXAMINED SKELETALLY 24950

| | NUMBER | | INCIDENCE PERCENT (RANGE) | | PROPORTIONAL (RANGE) |
|---|---------|---------|---------------------------|-------------|----------------------|
| | FETUSES | LITTERS | FETUSES | LITTERS | |
| EXTERNAL MALFORMATIONS | 7 | 7 | (0.0 - 0.4) | (0.0 - 5.0) | (0.0 - 0.4) |
| AGNATHIA (MANDIBULAR) | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.3) |
| GASTROSCHISIS | 9 | 9 | (0.0 - 0.4) | (0.0 - 5.0) | (0.0 - 1.7) |
| OMPHALOCELE | 4 | 4 | (0.0 - 0.4) | (0.0 - 5.0) | (0.0 - 0.5) |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | 3 | 3 | (0.0 - 0.3) | (0.0 - 5.0) | (0.0 - 0.3) |
| MULTIPLE ANOMALIES | 17 | 17 | (0.0 - 0.6) | (0.0 - 9.1) | (0.0 - 0.7) |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | 5 | 5 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| FETAL ANASARCA | 19 | 17 | (0.0 - 0.6) | (0.0 - 8.0) | (0.0 - 1.3) |
| MICROPTHALMIA AND/OR ANOPHTHALMIA | 6 | 6 | (0.0 - 0.3) | (0.0 - 5.3) | (0.0 - 0.3) |
| CLEFT PALATE | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.3) | (0.0 - 0.3) |
| BRACHYDACTYLY | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.3) |
| VERTEBRAL AGENESIS | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.3) |
| MICROGNATHIA (MANDIBULAR) | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.3) |
| CRANIORACHISCHISIS | 2 | 2 | (0.0 - 0.4) | (0.0 - 4.3) | (0.0 - 0.3) |
| ASTOMIA | 1 | 1 | (0.0 - 0.4) | (0.0 - 4.3) | (0.0 - 0.3) |
| CYCLOPIA | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| HYDROCEPHALY WITH OR WITHOUT DOME HEAD | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| MICROGNATHIA (MAXILLARY) | 5 | 5 | (0.0 - 0.4) | (0.0 - 4.8) | (0.0 - 0.4) |
| UMBILICAL HERNIATION OF INTESTINE | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.3) |
| MICROMELIA | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.3) | (0.0 - 0.3) |
| CEBOCEPHALY | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.3) |
| PINNA(E) - MALPOSITIONED | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.3) |
| LOCALIZED FETAL EDEMA | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.3) |

TOTAL NUMBER WITH EXTERNAL MALFORMATIONS 75 70

WIL HISTORICAL CONTROL DATA
CHARLES RIVER RATS CrlCD BR

SUMMARY INCIDENCE OF MALFORMATIONS
[INCLUDES PROPORTIONAL (PERCENT PER LITTER) DATA]

PAGE 3

TOTAL NUMBER OF LITTERS EXAMINED 2403

TOTAL NUMBER OF FETUSES EXAMINED EXTERNALLY 34139
TOTAL NUMBER OF FETUSES EXAMINED VISCERALLY 23712
TOTAL NUMBER OF FETUSES EXAMINED SKELETALLY 24950

| | NUMBER | | INCIDENCE PERCENT (RANGE) | | PROPORTIONAL (RANGE) |
|---|---------|---------|---------------------------|-------------|----------------------|
| | FETUSES | LITTERS | FETUSES | LITTERS | |
| SOFT TISSUE MALFORMATIONS | | | | | |
| ENCEPHALOMENINGOCELE | 3 | 2 | (0.0 - 1.3) | (0.0 - 5.0) | (0.0 - 1.3) |
| KIDNEY AND/OR URETER ABSENT | 3 | 3 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.4) |
| HEART AND/OR GREAT VESSEL ANOMALY | 11 | 7 | (0.0 - 1.8) | (0.0 - 5.0) | (0.0 - 1.9) |
| HYDROCEPHALY | 9 | 9 | (0.0 - 0.4) | (0.0 - 4.5) | (0.0 - 0.3) |
| TESTICULAR HYPOPLASIA | 1 | 1 | (0.0 - 0.3) | (0.0 - 5.0) | (0.0 - 0.3) |
| DIAPHRAGMATIC HERNIA | 2 | 2 | (0.0 - 0.7) | (0.0 - 5.0) | (0.0 - 0.7) |
| LOBULAR AGENESIS OF THE LUNG | 2 | 2 | (0.0 - 0.8) | (0.0 - 5.0) | (0.0 - 1.0) |
| MALPOSITIONED UTERUS | 1 | 1 | (0.0 - 0.7) | (0.0 - 5.0) | (0.0 - 0.8) |
| RETINA(S) FOLDED | 5 | 5 | (0.0 - 1.0) | (0.0 - 8.0) | (0.0 - 0.9) |
| SITUS INVERSUS | 10 | 10 | (0.0 - 0.6) | (0.0 - 8.0) | (0.0 - 0.5) |
| STENOTIC CAROTID(S) | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.3) | (0.0 - 0.4) |
| OVARY ABSENT | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.3) |
| UTERUS ABSENT | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.3) |
| TOTAL NUMBER WITH SOFT TISSUE MALFORMATIONS | 51 | 46 | | | |

WIL HISTORICAL CONTROL DATA
CHARLES RIVER RATS Cr1CD BR

SUMMARY INCIDENCE OF MALFORMATIONS
[INCLUDES PROPORTIONAL (PERCENT PER LITTER) DATA]

PAGE 4

TOTAL NUMBER OF LITTERS EXAMINED 2403

TOTAL NUMBER OF FETUSES EXAMINED EXTERNALLY 34139
TOTAL NUMBER OF FETUSES EXAMINED VISCERALLY 23712
TOTAL NUMBER OF FETUSES EXAMINED SKELETALLY 24950

| | NUMBER | | INCIDENCE PERCENT (RANGE) | | PROPORTIONAL (RANGE) |
|--|---------|--------|---------------------------|---------------|----------------------|
| | FETUSES | LITTER | FETUSES | LITTERS | % PER LITTER |
| SKELETAL MALFORMATIONS | 12 | 12 | (0.0 - 0.8) | (0.0 - 5.0) | (0.0 - 0.7) |
| VERTEBRAL ANOMALY WITH OR WITHOUT ASSOCIATED RIB ANOMALY | 3 | 3 | (0.0 - 0.6) | (0.0 - 4.8) | (0.0 - 0.3) |
| RIB ANOMALY | 2 | 2 | (0.0 - 0.6) | (0.0 - 4.5) | (0.0 - 0.5) |
| BENT LIMB BONE(S) | 3 | 3 | (0.0 - 0.6) | (0.0 - 4.8) | (0.0 - 0.7) |
| COSTAL CARTILAGE ANOMALY | 5 | 5 | (0.0 - 0.7) | (0.0 - 5.0) | (0.0 - 0.7) |
| STERNBRA(E) MALALIGNED (SEVERE) | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.7) |
| VERTEBRAL DYSGENESIS | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.3) |
| INTERRUPTED OSSIFICATION OF THE RIB(S) | 3 | 3 | (0.0 - 0.7) | (0.0 - 4.5) | (0.0 - 0.7) |
| RIB- HEMISPHERICAL ENLARGEMENT | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| SKULL ANOMALY | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| STERNOSCHISIS | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| VERTEBRAL AGENESIS | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.4) |
| TOTAL NUMBER WITH SKELETAL MALFORMATIONS | 33 | 33 | | | |

TOTAL NUMBER WITH MALFORMATIONS - TOTAL 140
- MEAN PERCENT 0.4 5.4

WIL HISTORICAL CONTROL DATA
CHARLES RIVER RATS CrLCD BR

SUMMARY INCIDENCE OF VARIATIONS
[INCLUDES PROPORTIONAL (PERCENT PER LITTER) DATA]

TOTAL NUMBER OF LITTERS EXAMINED 2403

TOTAL NUMBER OF FETUSES EXAMINED EXTERNALLY 34139

TOTAL NUMBER OF FETUSES EXAMINED VISCERALLY 23712

TOTAL NUMBER OF FETUSES EXAMINED SKELETALLY 24950

| | NUMBER | INCIDENCE PERCENT (RANGE) | | PROPORTIONAL (RANGE) | |
|----------------------------------|--------|---------------------------|---------------|----------------------|---------------|
| | | FETUSES | LITTERS | | FETUSES |
| EXTERNAL VARIATION | 5 | 5 | (0.0 - 1.0) | (0.0 - 13.6) | (0.0 - 0.9) |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.3) |
| TWINNING | | | | | |

| | NUMBER | INCIDENCE PERCENT (RANGE) | PROPORTIONAL (RANGE) |
|---|--------|---------------------------|----------------------|
| TOTAL NUMBER OF LITTERS EXAMINED | 2403 | | |
| TOTAL NUMBER OF FETUSES EXAMINED EXTERNALLY | 34139 | | |
| TOTAL NUMBER OF FETUSES EXAMINED VISCERALLY | 23712 | | |
| TOTAL NUMBER OF FETUSES EXAMINED SKELETALLY | 24950 | | |

| | FETUSES | LITTERS | FETUSES | LITTERS | % PER LITTER |
|---|---------|---------|----------------|----------------|----------------|
| SOFT TISSUES VARIATIONS | | | | | |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 308 | 229 | (0.0 - 10.9) | (0.0 - 34.1) | (0.0 - 14.2) |
| MAJOR BLOOD VESSEL VARIATION | 13 | 13 | (0.0 - 0.9) | (0.0 - 10.0) | (0.0 - 1.5) |
| DILATION OF THE ESOPHAGUS | 2 | 2 | (0.0 - 1.8) | (0.0 - 9.1) | (0.0 - 1.8) |
| HEMORRHAGIC KIDNEY(S) | 16 | 7 | (0.0 - 10.5) | (0.0 - 30.4) | (0.0 - 10.7) |
| DILATION OF THE BRAIN VENTRICLES | 9 | 6 | (0.0 - 5.9) | (0.0 - 26.1) | (0.0 - 6.6) |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | 1 | 1 | (0.0 - 0.7) | (0.0 - 4.3) | (0.0 - 0.7) |
| MISSHAPEN URETER | 1 | 1 | (0.0 - 0.5) | (0.0 - 3.7) | (0.0 - 0.5) |
| HEMORRHAGIC RING AROUND THE IRIS | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.3) |
| THYMUS HEMORRHAGIC | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.3) | (0.0 - 0.3) |
| BRAIN HEMORRHAGE | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.3) |
| KIDNEY(S)- CYST(S) | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.5) | (0.0 - 0.4) |

TOTAL NUMBER OF LITTERS EXAMINED 2403

TOTAL NUMBER OF FETUSES EXAMINED EXTERNALLY 34139
 TOTAL NUMBER OF FETUSES EXAMINED VISCERALLY 23712
 TOTAL NUMBER OF FETUSES EXAMINED SKELETALLY 24950

| | NUMBER | | INCIDENCE PERCENT (RANGE) | | PROPORTIONAL (RANGE) |
|--|---------|---------|---------------------------|----------------|----------------------|
| | FETUSES | LITTERS | FETUSES | LITTERS | |
| SKELETAL VARIATIONS | | | | | |
| STERNERA(E) #5 AND/OR #6 UNOSSIFIED | 3238 | 1244 | (0.6 - 36.6) | (4.5 -100.0) | (0.6 - 37.5) |
| HYOID UNOSSIFIED | 175 | 117 | (0.0 - 15.7) | (0.0 - 50.0) | (0.0 - 14.3) |
| 14TH RUDIMENTARY RIB(S) | 1349 | 634 | (0.0 - 38.9) | (0.0 - 94.7) | (0.0 - 39.3) |
| STERNERA(E) #1, #2, #3, AND/OR #4 UNOSSIFIED | 88 | 82 | (0.0 - 2.6) | (0.0 - 22.7) | (0.0 - 3.5) |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 331 | 229 | (0.0 - 11.1) | (0.0 - 36.0) | (0.0 - 11.5) |
| STERNERA(E) MALALIGNED(SLIGHT OR MODERATE) | 474 | 352 | (0.0 - 14.1) | (0.0 - 76.2) | (0.0 - 14.1) |
| REDUCED OSSIFICATION OF THE SKULL | 35 | 24 | (0.0 - 6.4) | (0.0 - 19.0) | (0.0 - 6.1) |
| 14TH FULL RIB(S) | 20 | 16 | (0.0 - 1.4) | (0.0 - 7.1) | (0.0 - 1.3) |
| 25 PRESACRAL VERTEBRAE | 45 | 32 | (0.0 - 4.0) | (0.0 - 22.7) | (0.0 - 3.8) |
| ENTIRE STERNUM UNOSSIFIED | 7 | 7 | (0.0 - 0.7) | (0.0 - 8.3) | (0.0 - 0.6) |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | 6 | 6 | (0.0 - 0.9) | (0.0 - 9.1) | (0.0 - 1.0) |
| 27 PRESACRAL VERTEBRAE | 48 | 31 | (0.0 - 4.4) | (0.0 - 18.2) | (0.0 - 4.2) |
| 7TH CERVICAL RIB(S) | 116 | 94 | (0.0 - 3.3) | (0.0 - 27.3) | (0.0 - 2.9) |
| REDUCED OSSIFICATION OF THE VERTERAL ARCHES | 28 | 26 | (0.0 - 1.9) | (0.0 - 10.0) | (0.0 - 1.7) |
| PUBIS UNOSSIFIED | 7 | 7 | (0.0 - 1.2) | (0.0 - 8.3) | (0.0 - 1.2) |
| BENT RIB(S) | 178 | 120 | (0.0 - 4.2) | (0.0 - 30.0) | (0.0 - 4.6) |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | 4 | 4 | (0.0 - 0.6) | (0.0 - 4.3) | (0.0 - 2.2) |
| REDUCED OSSIFICATION OF THE PELVIC GIRDL | 6 | 6 | (0.0 - 1.3) | (0.0 - 9.5) | (0.0 - 1.1) |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | 1 | 1 | (0.0 - 0.6) | (0.0 - 4.3) | (0.0 - 0.5) |
| ISCHIUM UNOSSIFIED | 2 | 2 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.5) |
| RIB(S) - THICKENED | 1 | 1 | (0.0 - 0.6) | (0.0 - 4.2) | (0.0 - 0.5) |
| REDUCED OSSIFICATION OF THE RIB(S) | 9 | 9 | (0.0 - 0.8) | (0.0 - 10.0) | (0.0 - 0.7) |
| CENTRA UNOSSIFIED | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.2) | (0.0 - 0.2) |
| CERVICAL CENTRUM #1 OSSIFIED | 599 | 190 | (0.0 - 19.2) | (0.0 - 80.0) | (0.0 - 20.3) |
| 14TH RUDIMENTARY RIB(S) WITH 15TH RUDIMENTARY RIB(S) | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.8) | (0.0 - 0.3) |
| UNCO-OSSIFIED VERTEBRAL CENTRA | 1 | 1 | (0.0 - 0.3) | (0.0 - 4.0) | (0.0 - 0.3) |

WIL-15218
Velsicol Chemical Corporation

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

APPENDIX C

WIL Historical Control Data (Sprague-Dawley CrI:CD®BR Rats) - Individual

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY

| STUDY NO. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 30 | 25 | 25 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 30 | 25 | 25 | 25 | 25 |
| NO. OF MINGRAVID: | 2 | 5 | 3 | 9 | 3 | 5 | 3 | 3 |
| NO. OF GRAVID: | 23 | 20 | 22 | 21 | 22 | 20 | 22 | 22 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 23 | 20 | 22 | 20 | 22 | 20 | 22 | 22 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 12.9(296) | 13.6(273) | 15.0(331) | 12.1(254) | 14.3(315) | 14.9(298) | 14.2(312) | 14.2(312) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.8(18) | 0.6(12) | 0.5(11) | 1.2(25) | 0.7(15) | 0.5(10) | 0.8(17) | 0.5(12) |
| POSTIMPLANTATION LOSS(% PER LITTER) | 5.7 | 4.3 | 3.5 | 8.4 | 4.6 | 3.7 | 5.2 | 3.7 |
| EARLY RESORPTIONS(% PER LITTER) | 5.4 | 4.3 | 3.5 | 8.2 | 4.0 | 3.7 | 5.2 | 3.7 |
| LATE RESORPTIONS(% PER LITTER) | 0.3 | 0.0 | 0.0 | 0.3 | 0.6 | 0.0 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER) | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM: | 13.7(314) | 14.3(285) | 15.5(342) | 13.3(279) | 15.0(330) | 15.4(308) | 15.0(329) | 14.7(324) |
| MEAN NO. OF CORPORA LUTEA/DAM: | 16.0(369) | 15.8(316) | 17.2(379) | 16.9(354) | 18.1(399) | 17.9(358) | 16.6(365) | 16.5(362) |
| FETAL SEX RATIO: MALE:FEMALE | 145:151 | 149:124 | 169:162 | 125:129 | 138:177 | 146:152 | 167:145 | 145:167 |
| % MALE | 49.0 | 54.6 | 51.1 | 49.2 | 43.8 | 49.0 | 53.5 | 46.5 |
| % FEMALE | 51.0 | 45.4 | 48.9 | 50.8 | 56.2 | 51.0 | 46.5 | 53.5 |
| MEAN FETAL BODY WEIGHT (G): | 3.3 | 3.4 | 3.4 | 3.4 | 3.3 | 3.4 | 3.4 | 3.6 |

DATE OF STUDY INITIATION: 09/01/82 07/20/82 08/02/82 03/29/82 04/13/82 08/10/82 07/27/82 09/19/82
 DATE OF STUDY TERMINATION: 10/05/82 08/14/82 08/27/82 05/14/82 05/23/82 09/10/82 08/23/82 11/17/82

VEHICLE NO.: 1 2 12 2 1 2 2 2 4

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 1,2 AND 4-8
 INTRAVAGINAL- STUDY NO. 3

VEHICLE NO. CODE: 1= CORN OIL 5= DEIONIZED WATER 9= INTRAVAGINAL PLACERO
 2= 0.5% METHYLCELLULOSE 6= STERILE WATER 10= 1% METHYLCELLULOSE
 3= DEOXYGENATED WATER 7= ENVIRONMENTAL CONTROL 11= CORN OIL / 1% TWEEN 80
 4= DISTILLED WATER 8= INTRAVAGINAL SHAM GAVAGE 12= 1% POLYVINYL ALCOHOL SOLUTION

106

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERCTOMY

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

| STUDY NO. | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 25 | 24a | 22 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 25 | 24 | 22 | 25 | 25 |
| NO. OF NONGRAVID: | 4 | 3 | 1 | 2 | 2 | 2 | 2 | 3 |
| NO. OF GRAVID: | 21 | 22 | 24 | 23 | 22 | 20 | 23 | 22 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 21 | 22 | 24 | 23 | 22 | 20 | 23 | 22 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 12.5(262) | 13.4(294) | 13.4(321) | 13.4(309) | 12.9(283) | 14.1(282) | 13.5(311) | 13.7(301) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.7(15) | 0.5(11) | 0.8(19) | 0.5(11) | 0.5(11) | 0.4(8) | 0.8(19) | 0.7(16) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 5.1 | 3.4 | 5.5 | 3.5 | 4.2 | 2.8 | 5.2 | 4.9 |
| EARLY RESORPTIONS(% PER LITTER): | 4.7 | 3.4 | 5.5 | 3.5 | 4.2 | 2.8 | 5.2 | 4.9 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM: | 13.2(277) | 13.9(305) | 14.2(340) | 13.9(320) | 13.4(294) | 14.5(290) | 14.3(330) | 14.4(317) |
| MEAN NO. OF CORPORA LUTEA/DAM: | 16.6(348) | 15.2(335) | 15.8(378) | 16.6(348) | 14.5(320) | 16.0(320) | 15.8(364) | 15.7(346) |
| FETAL SEX RATIO: MALE:FEMALE | 132:130 | 142:152 | 160:161 | 173:136 | 147:136 | 137:145 | 152:159 | 152:149 |
| % MALE | 50.4 | 48.3 | 49.8 | 56.0 | 51.9 | 48.6 | 48.9 | 50.5 |
| % FEMALE | 49.6 | 51.7 | 50.2 | 44.0 | 48.1 | 51.4 | 51.1 | 49.5 |
| MEAN FETAL BODY WEIGHT (G): | 3.3 | 3.3 | 3.5 | 3.5 | 3.4 | 3.5 | 3.5 | 3.4 |

DATE OF STUDY INITIATION: 09/30/82 06/15/83 03/23/83 09/01/82 05/24/83 05/17/83 05/24/83 09/07/83
 DATE OF STUDY TERMINATION: 10/27/82 07/08/83 04/20/83 10/02/82 06/24/83 06/09/83 06/18/83 10/03/83

VEHICLE NO.: 4 5 1 2 1 2 1 1 5/2b

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 9-16

VEHICLE NO. CODE: 1= CORN OIL 5= DEIONIZED WATER 9= INTRAVAGINAL PLACERO
 2= 0.5% METHYLCELLULOSE 6= STERILE WATER 10= 1% METHYLCELLULOSE
 3= DEOXYGENATED WATER 7= ENVIRONMENTAL CONTROL 11= CORN OIL / 1% TWEEN 80
 4= DISTILLED WATER 8= INTRAVAGINAL SHAM GAVAGE 12= 1% POLYVINYL ALCOHOL SOLUTION

a = DOES NOT INCLUDE ONE FEMALE WHICH DELIVERED PRIOR TO SCHEDULED CESAREAN SECTION DUE TO AN ERROR IN DETECTION OF MATING

b = CONTROL ANIMALS RECEIVED DEIONIZED WATER IMMEDIATELY FOLLOWED BY 0.5% METHYLCELLULOSE

MATERNAL AND FETAL OBSERVATIONS AT LAPAROSTERECTOMY

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

| STUDY NO. | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 25 | 30 | 30 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 25 | 30 | 30 | 25 | 25 |
| NO. OF NONGRAVID: | 0 | 3 | 1 | 1 | 2 | 3 | 0 | 3 |
| NO. OF GRAVID: | 25 | 22 | 24 | 24 | 28 | 27 | 25 | 22 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 25 | 22 | 24 | 24 | 28 | 27 | 25 | 22 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 14.4(360) | 13.8(303) | 15.4(370) | 14.1(338) | 14.4(403) | 14.3(385) | 15.1(378) | 14.4(316) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.6(15) | 0.5(10) | 0.5(11) | 0.7(16) | 0.6(17) | 0.8(21) | 0.5(12) | 0.6(14) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 4.1 | 2.9 | 2.7 | 4.7 | 4.3 | 5.3 | 3.1 | 4.0 |
| EARLY RESORPTIONS(% PER LITTER): | 4.1 | 2.9 | 2.7 | 4.4 | 4.0 | 4.8 | 3.1 | 4.0 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.2 | 0.2 | 0.5 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 15.0(375) | 14.2(313) | 15.9(381) | 14.8(354) | 15.0(420) | 15.0(406) | 15.6(390) | 15.0(330) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 16.4(409) | 16.1(355) | 17.1(410) | 16.3(391) | 15.9(446) | 16.6(448) | 16.1(402) | 16.1(354) |
| FETAL SEX RATIO: MALE:FEMALE | 186:174 | 153:150 | 186:184 | 165:173 | 190:213 | 190:195 | 188:190 | 156:160 |
| % MALE | 51.7 | 50.5 | 50.3 | 48.8 | 47.1 | 49.4 | 49.7 | 49.4 |
| % FEMALE | 48.3 | 49.5 | 49.7 | 51.2 | 52.9 | 50.6 | 50.3 | 50.6 |
| MEAN FETAL BODY WEIGHT (G): | 3.6 | 3.5 | 3.6 | 3.7 | 3.6 | 3.5 | 3.7 | 3.4 |

DATE OF STUDY INITIATION: 11/09/83 11/09/83 11/09/83 01/10/84 09/05/84 07/17/84 10/02/84 12/20/84
DATE OF STUDY TERMINATION: 12/02/83 12/02/83 12/02/83 02/05/84 09/28/84 08/10/84 10/27/84 01/14/85

VEHICLE NO.: 9 7 8 1 6 1 1 1 c

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 20, 22-24
INTRAVAGINAL- STUDY NO. 17-19
SUBCUTANEOUS INJECTION- STUDY NO. 21

VEHICLE NO. CODE: 1= CORN OIL 5= DEIONIZED WATER 9= INTRAVAGINAL PLACEBO
2= 0.5% METHYLCELLULOSE 6= STERILE WATER 10= 1% METHYLCELLULOSE
3= DEOXYGENATED WATER 7= ENVIRONMENTAL CONTROL 11= CORN OIL / 1% TWEEN 80
4= DISTILLED WATER 8= INTRAVAGINAL SHAM GAVAGE 12= 1% POLYVINYL ALCOHOL SOLUTION

VIL INDIVIDUAL HISTORICAL CONTROL DATA MATERNAL AND FETAL OBSERVATIONS AT LAPAROSTERECTOMY PAGE 4
 CHARLES RIVER CD RATS

| STUDY NO. | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 45 | 25 | 25 | 25 | 25 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 45 | 25 | 25 | 25 | 25 | 25 | 25 |
| NO. OF NONGRAVID: | 4 | 4 | 2 | 1 | 3 | 5 | 3 | 9 |
| NO. OF GRAVID: | 21 | 41 | 23 | 24 | 22 | 20 | 22 | 16 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 20 | 41 | 23 | 24 | 22 | 20 | 22 | 16 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 15.0(314) | 13.9(570) | 13.6(313) | 15.0(361) | 14.2(312) | 12.9(257) | 15.3(336) | 14.1(225) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 1.0(22) | 0.4(15) | 0.7(16) | 0.8(20) | 0.7(16) | 1.0(19) | 0.8(17) | 0.8(13) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 10.5 | 2.7 | 4.7 | 5.0 | 5.1 | 7.8 | 4.9 | 5.5 |
| EARLY RESORPTIONS(% PER LITTER): | 10.3 | 2.7 | 4.7 | 5.0 | 5.1 | 7.5 | 4.9 | 5.5 |
| LATE RESORPTIONS(% PER LITTER): | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 16.0(336) | 14.3(585) | 14.3(329) | 15.9(381) | 14.9(328) | 13.8(276) | 16.0(353) | 14.9(238) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 16.7(351) | 15.6(640) | 15.7(361) | 16.5(395) | 16.4(360) | 17.6(353) | 18.1(399) | 16.4(262) |
| FETAL SEX RATIO: MALE:FEMALE | 151:163 | 269:301 | 157:156 | 150:211 | 160:152 | 131:126 | 140:196 | 117:108 |
| % MALE | 48.1 | 47.2 | 50.2 | 41.6 | 51.3 | 51.0 | 41.7 | 52.0 |
| % FEMALE | 51.9 | 52.8 | 49.8 | 58.4 | 48.7 | 49.0 | 58.3 | 48.0 |
| MEAN FETAL BODY WEIGHT (G): | 3.6 | 3.6 | 3.4 | 3.6 | 3.5 | 3.4 | 3.5 | 3.6 |

DATE OF STUDY INITIATION: 11/06/84 02/06/85 12/13/84 09/25/84 01/03/85 02/19/85 04/02/85 08/28/85
 DATE OF STUDY TERMINATION: 11/29/84 03/08/85 01/09/85 10/19/84 01/26/85 03/19/85 04/25/85 10/01/85

VEHICLE NO.: NA 1 5 1 1 10 1 1 1 1

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 26-32
 DIETARY- STUDY NO. 25

VEHICLE NO. CODE: 1= CORN OIL 5= DEIONIZED WATER 9= INTRAVAGINAL PLACEBO
 2= 0.5% METHYLCELLULOSE 6= STERILE WATER 10= 1% METHYLCELLULOSE
 3= DEOXYGENATED WATER 7= ENVIRONMENTAL CONTROL 11= CORN OIL / 1% TWEEN 80
 4= DISTILLED WATER 8= INTRAVAGINAL SHAM GAVAGE 12= 1% POLYVINYL ALCOHOL SOLUTION

VII. INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY

| STUDY NO. | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 10 | 25 | 25 | 10 | 25 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 10 | 25 | 25 | 10 | 25 | 25 | 25 |
| NO. OF NONGRAVID: | 2 | 0 | 2 | 1 | 0 | 5 | 4 | 2 |
| NO. OF GRAVID: | 23 | 10 | 23 | 24 | 10 | 20 | 21 | 23 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 23 | 10 | 23 | 24 | 10 | 20 | 21 | 23 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 13.6(312) | 14.0(140) | 15.2(349) | 14.0(335) | 16.1(161) | 15.9(317) | 14.6(307) | 15.5(356) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 1.0(23) | 1.0(10) | 0.8(18) | 0.9(22) | 0.6(6) | 0.7(14) | 1.0(21) | 0.9(20) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 6.8 | 7.6 | 4.7 | 6.2 | 3.7 | 4.1 | 6.3 | 5.4 |
| EARLY RESORPTIONS(% PER LITTER): | 6.8 | 7.6 | 4.7 | 6.2 | 3.7 | 3.8 | 6.3 | 5.4 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 14.6(335) | 15.0(150) | 16.0(367) | 14.9(357) | 16.7(167) | 16.6(331) | 15.6(328) | 16.3(376) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 17.7(407) | 17.2(172) | 16.9(388) | 16.3(390) | 18.8(188) | 17.6(352) | 16.9(354) | 17.7(407) |
| FETAL SEX RATIO: MALE:FEMALE | 161:151 | 62:78 | 166:183 | 159:176 | 76:85 | 167:150 | 156:151 | 180:176 |
| % MALE | 51.6 | 44.3 | 47.6 | 47.5 | 47.2 | 52.7 | 50.8 | 50.6 |
| % FEMALE | 48.4 | 55.7 | 52.4 | 52.5 | 52.8 | 47.3 | 49.2 | 49.4 |
| MEAN FETAL BODY WEIGHT (G): | 3.5 | 3.6 | 3.5 | 3.6 | 3.7 | 3.7 | 3.5 | 3.4 |

DATE OF STUDY INITIATION:
DATE OF STUDY TERMINATION:

10/29/85 11/18/85 06/25/85 04/01/86 01/27/86 05/06/86 07/02/85 06/18/85
11/25/85 12/12/85 07/20/85 04/28/86 02/20/86 05/30/86 07/26/85 07/12/85

VEHICLE NO.:

1 1 1 1 1 1 1 2 1

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 33-40

VEHICLE NO. CODE: 1- CORN OIL 5- DEIONIZED WATER 9- INTRAVAGINAL PLACEBO
2- 0.5% METHYLCELLULOSE 6- STERILE WATER 10- 1% METHYLCELLULOSE
3- DEOXYGENATED WATER 7- ENVIRONMENTAL CONTROL 11- CORN OIL / 1% TWEEN 80
4- DISTILLED WATER 8- INTRAVAGINAL SHAM GAVAGE 12- 1% POLYVINYL ALCOHOL SOLUTION

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

| STUDY NO. | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| NO. OF NONGRAVID: | 3 | 1 | 2 | 3 | 3 | 1 | 6 | 3 |
| NO. OF GRAVID: | 22 | 24 | 23 | 22 | 22 | 24 | 19 | 22 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 22 | 24 | 23 | 22 | 22 | 24 | 19 | 22 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 14.0(308) | 15.4(369) | 14.3(329) | 14.2(313) | 14.0(308) | 14.0(336) | 14.2(270) | 14.0(307) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.7(16) | 0.6(15) | 0.9(21) | 0.7(15) | 0.8(17) | 1.1(27) | 0.5(9) | 0.8(18) |
| POSTIMPLANTATION LOSSES/DAM(% PER LITTER): | 4.7 | 3.9 | 6.3 | 4.4 | 5.4 | 7.4 | 3.4 | 5.1 |
| EARLY RESORPTIONS(% PER LITTER): | 4.7 | 3.9 | 6.3 | 4.4 | 5.4 | 7.4 | 3.0 | 5.1 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 14.7(324) | 16.0(384) | 15.2(350) | 14.9(328) | 14.8(325) | 15.1(363) | 14.7(279) | 14.8(325) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 16.4(360) | 17.2(413) | 16.5(379) | 16.3(359) | 16.0(352) | 16.0(385) | 16.6(315) | 16.6(366) |
| FETAL SEX RATIO: MALE:FEMALE | 174:134 | 194:175 | 156:173 | 166:147 | 159:149 | 172:164 | 137:133 | 149:158 |
| % MALE | 56.5 | 52.6 | 47.4 | 53.0 | 51.6 | 51.2 | 50.7 | 48.5 |
| % FEMALE | 43.5 | 47.4 | 52.6 | 47.0 | 48.4 | 48.8 | 49.3 | 51.5 |
| MEAN FETAL BODY WEIGHT (G): | 3.4 | 3.6 | 3.5 | 3.6 | 3.5 | 3.5 | 3.3 | 3.5 |

| | | | | | | | | |
|----------------------------|----------|----------|----------|----------|----------|----------|----------|----------|
| DATE OF STUDY INITIATION: | 02/11/86 | 02/18/86 | 11/20/86 | 08/26/86 | 11/24/86 | 11/19/86 | 09/09/86 | 06/18/85 |
| DATE OF STUDY TERMINATION: | 03/15/86 | 03/13/86 | 12/13/86 | 09/20/86 | 12/17/86 | 12/13/86 | 10/04/86 | 07/11/85 |

| | | | | | | | | |
|--------------|----|---|---|---|---|----|---|---|
| VEHICLE NO.: | 10 | 1 | 1 | 1 | 3 | 11 | 2 | 1 |
|--------------|----|---|---|---|---|----|---|---|

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 41-48

| | | | |
|-------------------|-------------------------|-----------------------------|-----------------------------------|
| VEHICLE NO. CODE: | 1- CORN OIL | 5- DEIONIZED WATER | 9- INTRAVAGINAL PLACERO |
| | 2- 0.5% METHYLCELLULOSE | 6- STERILE WATER | 10- 1% METHYLCELLULOSE |
| | 3- DEOXYGENATED WATER | 7- ENVIRONMENTAL CONTROL | 11- CORN OIL / 1% TWEEN 80 |
| | 4- DISTILLED WATER | 8- INTRAVAGINAL SHAM GAVAGE | 12- 1% POLYVINYL ALCOHOL SOLUTION |

WIL INDIVIDUAL HISTORICAL CONTROL DATA MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY PAGE 7
 CHARLES RIVER CD RATS

| STUDY NO. | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 24 | 24 | 15 | 25 | 25 | 25 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 24 | 24 | 15 | 25 | 25 | 25 | 25 | 24 |
| NO. OF NONGRAVID: | 0 | 3 | 1 | 3 | 10 | 5 | 2 | 4 |
| NO. OF GRAVID: | 24 | 21 | 14 | 22 | 15 | 20 | 23 | 20 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 24 | 21 | 14 | 22 | 15 | 20 | 23 | 20 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 13.3(318) | 13.0(273) | 14.5(203) | 14.6(321) | 12.1(182) | 14.6(292) | 14.2(326) | 13.0(260) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.7(17) | 0.9(18) | 1.1(15) | 1.0(21) | 0.3(5) | 1.1(21) | 1.0(22) | 0.9(18) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 5.0 | 7.2 | 6.7 | 5.6 | 2.2 | 6.7 | 6.3 | 6.2 |
| EARLY RESORPTIONS(% PER LITTER): | 5.0 | 6.0 | 6.2 | 5.1 | 1.8 | 6.7 | 6.3 | 5.9 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 1.2 | 0.5 | 0.5 | 0.4 | 0.0 | 0.0 | 0.3 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 14.0(335) | 13.9(291) | 15.6(218) | 15.5(342) | 12.5(187) | 15.7(313) | 15.1(348) | 13.9(278) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 15.8(380) | 16.0(337) | 17.7(248) | 19.2(422) | 14.5(217) | 17.0(339) | 16.7(385) | 14.7(294) |
| FETAL SEX RATIO: MALE:FEMALE | 147:171 | 128:145 | 92:111 | 159:162 | 79:103 | 143:149 | 168:158 | 115:145 |
| % MALE | 46.2 | 46.9 | 45.3 | 49.5 | 43.4 | 49.0 | 51.5 | 44.2 |
| % FEMALE | 53.8 | 53.1 | 54.7 | 50.5 | 56.6 | 51.0 | 48.5 | 55.8 |
| MEAN FETAL BODY WEIGHT (G): | 3.6 | 3.5 | 3.5 | 3.7 | 3.5 | 3.6 | 3.5 | 3.4 |

DATE OF STUDY INITIATION: 05/15/86 07/10/85 01/05/87 02/09/87 11/24/86 02/17/87 01/22/85
 DATE OF STUDY TERMINATION: 09/24/86 09/24/86 03/31/86 01/28/87 03/05/87 12/18/86 03/12/87 02/17/85

VEHICLE NO.: 6 (d) 5 5 5 5 1 5 5 1

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 49-56

- VEHICLE NO. CODE: 1= CORN OIL 5= DEIONIZED WATER 9= INTRAVAGINAL PLACERO
 2= 0.5% METHYLCELLULOSE 6= STERILE WATER 10= 1% METHYLCELLULOSE
 3= DEOXYGENATED WATER 7= ENVIRONMENTAL CONTROL 11= CORN OIL / 1% TWEEN 80
 4= DISTILLED WATER 8= INTRAVAGINAL SHAM GAVAGE 12= 1% POLYVINYL ALCOHOL SOLUTION

(d) = UNTREATED CONTROL

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY

| STUDY NO. | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 25 | 25 | 28 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 25 | 25 | 28 | 25 | 25 |
| NO. OF NONGRAVID: | 0 | 1 | 0 | 5 | 0 | 3 | 6 | 2 |
| NO. OF GRAVID: | 25 | 24 | 25 | 20 | 25 | 25 | 19 | 23 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 |
| NO. OF DAMS WITH LIVE FETUSES: | 25 | 24 | 25 | 20 | 25 | 23 | 19 | 22 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 14.2(355) | 13.1(315) | 12.4(311) | 15.0(299) | 14.6(364) | 10.7(268) | 16.5(313) | 15.2(349) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.6(15) | 0.8(20) | 1.2(29) | 0.7(13) | 0.4(11) | 0.8(20) | 0.9(18) | 0.7(16) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 4.1 | 6.8 | 9.1 | 4.1 | 3.1 | 13.5 | 5.5 | 8.3 |
| EARLY RESORPTIONS(% PER LITTER): | 4.1 | 6.8 | 9.1 | 4.1 | 3.1 | 13.5 | 5.5 | 8.3 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 14.8(370) | 14.0(335) | 13.6(340) | 15.6(312) | 15.0(375) | 11.5(288) | 17.4(331) | 15.9(365) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 16.0(401) | 15.8(380) | 15.7(392) | 16.7(333) | 16.6(414) | 14.4(359) | 18.8(357) | 17.8(409) |
| FETAL SEX RATIO: MALE:FEMALE | 172:183 | 147:168 | 138:173 | 163:136 | 157:207 | 140:128 | 150:163 | 194:155 |
| % MALE | 48.5 | 46.7 | 44.4 | 54.5 | 43.1 | 52.2 | 47.9 | 55.6 |
| % FEMALE | 51.5 | 53.3 | 55.6 | 45.5 | 56.9 | 47.8 | 52.1 | 44.4 |
| MEAN FETAL BODY WEIGHT (G): | 3.4 | 3.4 | 3.4 | 3.6 | 3.6 | 3.4 | 3.8 | 3.4 |

DATE OF STUDY INITIATION: 07/26/88 06/07/88 07/12/88 09/27/88 09/09/86 02/16/88 01/10/89 06/21/88
DATE OF STUDY TERMINATION: 08/21/88 07/02/88 08/06/88 10/21/88 10/03/86 11/06/88 02/06/89 07/19/88

VEHICLE NO.: 5 5 5 1 5 5 5 5 1 14 1

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 57-62,64
INTRAVENOUS INJECTION- STUDY NO. 63

VEHICLE NO. CODE: 1= CORN OIL 7= ENVIRONMENTAL CONTROL 13= 0.2% HYDROXYPROPYLMETHYLCELLULOSE
2= 0.5% METHYLCELLULOSE 8= INTRAVAGINAL SHAM GAVAGE
3= DEOXYGENATED WATER 9= INTRAVAGINAL PLACEDO
4= DISTILLED WATER 10= 1% METHYLCELLULOSE
5= DEIONIZED WATER 11= CORN OIL / 1 % TWEEN 80
6= STERILE WATER 12= 1% POLYVINYL ALCOHOL SOLUTION

| STUDY NO. | 65 | 66 | 67 | 68 | 69 | 70 | 71 | 72 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 23 | 25 | 25 | 25 | 21 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 23 | 25 | 25 | 25 | 21 | 25 |
| NO. OF NONGRAVID: | 3 | 3 | 2 | 1 | 1 | 4 | 1 | 6 |
| NO. OF GRAVID: | 22 | 22 | 21 | 24 | 24 | 21 | 20 | 19 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 22 | 22 | 21 | 24 | 24 | 21 | 20 | 19 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 14.9(328) | 14.9(327) | 13.8(289) | 13.0(311) | 14.8(356) | 14.4(303) | 14.9(298) | 15.7(298) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.5(12) | 1.0(21) | 0.8(17) | 1.3(32) | 0.9(21) | 1.0(20) | 0.9(17) | 0.9(18) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 3.3 | 6.6 | 5.7 | 9.5 | 7.0 | 5.9 | 5.3 | 5.7 |
| EARLY RESORPTIONS(% PER LITTER): | 3.0 | 6.3 | 5.3 | 9.3 | 7.0 | 5.6 | 5.3 | 5.7 |
| LATE RESORPTIONS(% PER LITTER): | 0.3 | 0.3 | 0.3 | 0.3 | 0.0 | 0.3 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 15.5(340) | 15.8(348) | 14.6(306) | 14.3(343) | 15.7(377) | 15.4(323) | 15.8(315) | 16.6(316) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 17.7(390) | 16.9(371) | 15.4(324) | 15.8(379) | 18.4(442) | 16.4(345) | 17.3(345) | 18.5(351) |
| FETAL SEX RATIO: MALE:FEMALE | 170:158 | 148:179 | 134:155 | 152:159 | 172:184 | 148:155 | 136:162 | 169:129 |
| % MALE | 51.8 | 45.3 | 46.4 | 48.9 | 48.3 | 48.8 | 45.6 | 56.7 |
| % FEMALE | 48.2 | 54.7 | 53.6 | 51.1 | 51.7 | 51.2 | 54.4 | 43.3 |
| MEAN FETAL BODY WEIGHT (G): | 3.6 | 3.6 | 3.5 | 3.6 | 3.7 | 3.6 | 3.6 | 3.8 |

DATE OF STUDY INITIATION:
DATE OF STUDY TERMINATION:

| | | | | | | | |
|----------|----------|----------|----------|----------|----------|----------|----------|
| 02/08/89 | 08/24/88 | 07/22/88 | 06/21/89 | 05/10/89 | 10/11/88 | 05/18/88 | 05/25/89 |
| 03/05/89 | 12/10/88 | 01/19/89 | 07/15/89 | 06/08/89 | 03/17/89 | 10/25/88 | 06/21/89 |

VEHICLE NO.:

| | | | | | | | |
|---|----|----|---|---|----|---|---|
| 5 | 15 | 15 | 1 | 1 | 16 | 2 | 1 |
|---|----|----|---|---|----|---|---|

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NO.'S 65-69, 71, 72
INTRAVENOUS INJECTION- STUDY NO. 70

| VEHICLE NO. CODE: | 1= CORN OIL | 7= ENVIRONMENTAL CONTROL | 13= 0.2% HYDROXYPROPYLMETHYLCELLULOSE |
|-------------------------|-----------------------------------|--|---------------------------------------|
| 2= 0.5% METHYLCELLULOSE | 8= INTRAVAGINAL SHAM GAVAGE | 14= 0.9% SODIUM CHLORIDE SOLUTION | |
| 3= DEOXYGENATED WATER | 9= INTRAVAGINAL PLACEBO | 15= 0.4% METHYLCELLULOSE | |
| 4= DISTILLED WATER | 10= 1% METHYLCELLULOSE | 16= SPONSOR SUPPLIED CONTROL FORMULATION | |
| 5= DEIONIZED WATER | 11= CORN OIL / 1 % TWEEN 80 | | |
| 6= STERILE WATER | 12= 1% POLYVINYL ALCOHOL SOLUTION | | |

204

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

| STUDY NO. | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 25 | 25 | 25 | 23 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 25 | 25 | 25 | 23 | 25 |
| NO. OF NONGRAVID: | 3 | 4 | 1 | 1 | 1 | 2 | 0 | 2 |
| NO. OF GRAVID: | 22 | 21 | 24 | 24 | 24 | 23 | 23 | 23 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 22 | 21 | 24 | 23 | 24 | 22 | 23 | 23 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 13.8(303) | 14.5(304) | 13.5(325) | 13.3(320) | 14.4(345) | 14.5(319) | 12.4(286) | 14.0(321) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.7(15) | 1.0(21) | 0.7(16) | 0.9(22) | 0.7(16) | 1.3(31) | 0.8(18) | 0.8(18) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 4.8 | 6.7 | 6.0 | 10.3 | 4.1 | 10.1 | 7.5 | 5.1 |
| EARLY RESORPTIONS(% PER LITTER): | 4.8 | 6.7 | 6.0 | 10.3 | 3.9 | 6.9 | 7.5 | 5.1 |
| LATE RESORPTIONS(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 3.2 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 14.5(318) | 15.5(325) | 14.2(341) | 14.3(342) | 15.0(361) | 15.2(350) | 13.2(304) | 14.7(339) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 15.8(348) | 16.7(351) | 15.7(376) | 16.1(387) | 16.7(401) | 17.5(402) | 15.6(359) | 15.8(363) |
| FETAL SEX RATIO: MALE:FEMALE | 154:149 | 135:169 | 151:174 | 156:164 | 167:178 | 158:161 | 141:145 | 151:170 |
| % MALE | 50.8 | 44.4 | 46.5 | 48.8 | 48.4 | 49.5 | 49.3 | 47.0 |
| % FEMALE | 49.2 | 55.6 | 53.5 | 51.3 | 51.6 | 50.5 | 50.7 | 53.0 |
| MEAN FETAL BODY WEIGHT (G): | 3.7 | 3.5 | 3.5 | 3.6 | 3.7 | 3.7 | 3.4 | 3.5 |

DATE OF STUDY INITIATION:
DATE OF STUDY TERMINATION:

| | | | | | | | |
|----------|----------|----------|----------|----------|----------|----------|----------|
| 10/10/89 | 11/21/89 | 09/27/89 | 11/28/89 | 02/06/90 | 02/13/90 | 07/13/89 | 04/03/90 |
| 11/02/89 | 12/17/89 | 10/24/89 | 12/30/89 | 03/03/90 | 03/09/90 | 11/23/89 | 04/27/90 |

VEHICLE NO.:

| | | | | | | | |
|---|----|---|---|---|---|---|---|
| 5 | 10 | 1 | 2 | 1 | 1 | 4 | 5 |
|---|----|---|---|---|---|---|---|

ROUTE OF ADMINISTRATION: ORAL BY CAVAGE- STUDY NOS. 73-80

| VEHICLE NO. CODE: | 1= CORN OIL | 7= ENVIRONMENTAL CONTROL | 13= 0.2% HYDROXYPROPYLMETHYLCELLULOSE |
|-------------------------|-----------------------------|-----------------------------------|--|
| 2= 0.5% METHYLCELLULOSE | 8= INTRAVAGINAL SHAM CAVAGE | 14= 0.9% SODIUM CHLORIDE SOLUTION | 15= 0.4% METHYLCELLULOSE |
| 3= DEOXYGENATED WATER | 9= INTRAVAGINAL PLACERO | 15= 0.4% METHYLCELLULOSE | 16= SPONSOR SUPPLIED CONTROL FORMULATION |
| 4= DISTILLED WATER | 10= 1% METHYLCELLULOSE | | |
| 5= DEIONIZED WATER | 11= CORN OIL / 1 % TWEEN 80 | | |

MATERNAL AND FETAL OBSERVATIONS AT LAPAROHYSTERECTOMY

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

STUDY NO. 89 90 91 92 93 94 95 96

NO. OF ANIMALS IN THE CONTROL GROUP: 25 24 24 25 24 24 25 25 25

NO. OF ANIMALS THAT DIED: 0 0 0 0 0 0 0 0 0

NO. OF ANIMALS THAT ABORTED/DELIVERED: 0 0 0 0 0 0 0 0 0

NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: 25 24 24 25 24 24 25 25 25

NO. OF NONGRAVID: 4 1 3 3 1 3 5 5 0

NO. OF GRAVID: 21 24 21 22 23 21 20 25 25

NO. OF DAMS WITH ONLY RESORPTIONS: 0 0 0 0 0 0 0 0 0

NO. OF DAMS WITH LIVE FETUSES: 21 24 21 22 23 21 20 25 25

MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): 13.5(284) 14.4(345) 16.0(336) 15.0(329) 15.4(355) 15.2(320) 13.3(266) 14.1(353)

MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): 0.7(14) 0.7(16) 0.6(13) 0.9(19) 1.0(22) 0.9(18) 0.7(13) 0.6(16)

POSTIMPLANTATION LOSS(% PER LITTER): 4.7 4.4 5.6 5.5 6.0 5.4 5.0 4.4

EARLY RESORPTIONS(% PER LITTER): 4.4 4.2 5.3 5.5 6.0 4.9 4.7 4.4

LATE RESORPTIONS(% PER LITTER): 0.3 0.3 0.3 0.0 0.0 0.5 0.4 0.0

DEAD FETUSES(% PER LITTER): 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0

MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): 14.2(298) 15.0(361) 16.6(349) 15.8(348) 16.4(377) 16.1(338) 14.0(279) 14.8(369)

MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): 15.3(322) 16.1(387) 18.2(382) 17.8(392) 17.0(392) 17.6(370) 16.7(333) 15.7(393)

FETAL SEX RATIO: MALE:FEMALE 123:161 162:183 159:177 164:165 184:171 172:148 132:134 179:174

% MALE 43.3 47.0 47.3 49.8 51.8 53.8 49.6 50.7

% FEMALE 56.7 53.0 52.7 50.2 48.2 46.3 50.4 49.3

MEAN FETAL BODY WEIGHT (G): 3.5 3.5 3.6 3.5 3.7 3.7 3.5 3.5

DATE OF STUDY INITIATION: 03/27/90 08/07/90 11/27/90 01/29/91 03/26/91 04/23/91 01/03/90 04/24/90

DATE OF STUDY TERMINATION: 04/22/90 08/31/90 12/20/90 02/22/91 04/18/91 05/18/91 01/27/90 05/17/90

VEHICLE NO.: 4 1 18 4 18 18 1 1

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NOS. 89, 90, 92, 95 AND 96
INHALATION- STUDY NOS. 91, 93 AND 94

VEHICLE NO. CODE: 1= CORN OIL 7= ENVIRONMENTAL CONTROL 13= 0.2% HYDROXYPROPYLMETHYLCELLULOSE
2= 0.5% METHYLCELLULOSE 8= INTRAVAGINAL SHAM GAVAGE 14= 0.9% SODIUM CHLORIDE SOLUTION
3= DEOXYGENATED WATER 9= INTRAVAGINAL PLACEBO 15= 0.4% METHYLCELLULOSE
4= DISTILLED WATER 10= 1% METHYLCELLULOSE 16= SPONSOR SUPPLIED CONTROL FORMULATION
5= DEIONIZED WATER 11= CORN OIL / 1 % TWEEN 80 17= OLIVE OIL
6= STERILE WATER 12= 1% POLYVINYL ALCOHOL SOLUTION 18= CLEAN, FILTERED AIR

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY

| STUDY NO. | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| NO. OF ANIMALS IN THE CONTROL GROUP: | 25 | 25 | 25 | 23 | 23 | 25 | 25 | 25 |
| NO. OF ANIMALS THAT DIED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS THAT ABORTED/DELIVERED: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: | 25 | 25 | 25 | 23 | 23 | 25 | 25 | 25 |
| NO. OF NONGRAVID: | 1 | 2 | 2 | 0 | 3 | 0 | 1 | 0 |
| NO. OF GRAVID: | 24 | 23 | 23 | 23 | 20 | 25 | 24 | 25 |
| NO. OF DAMS WITH ONLY RESORPTIONS: | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| NO. OF DAMS WITH LIVE FETUSES: | 24 | 23 | 23 | 23 | 20 | 25 | 24 | 25 |
| MEAN NO. VIABLE FETUSES/DAM(TOTAL NO.): | 13.7(328) | 14.7(339) | 13.9(319) | 13.9(320) | 14.4(287) | 13.9(347) | 16.0(385) | 13.6(339) |
| MEAN NO. POSTIMPLANTATION LOSSES/DAM(TOTAL NO.): | 0.6(15) | 0.7(15) | 0.6(13) | 0.5(12) | 1.1(22) | 0.8(21) | 1.2(29) | 1.1(27) |
| POSTIMPLANTATION LOSS(% PER LITTER): | 4.2 | 4.3 | 4.3 | 3.6 | 7.2 | 5.3 | 7.2 | 7.0 |
| EARLY RESORPTIONS(% PER LITTER): | 3.9 | 4.3 | 4.3 | 3.3 | 6.8 | 5.3 | 7.2 | 7.0 |
| LATE RESORPTIONS(% PER LITTER): | 0.3 | 0.0 | 0.0 | 0.3 | 0.4 | 0.0 | 0.0 | 0.0 |
| DEAD FETUSES(% PER LITTER): | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN NO. OF IMPLANTATIONS/DAM(TOTAL NO.): | 14.3(343) | 15.4(354) | 14.4(332) | 14.4(332) | 15.5(309) | 14.7(368) | 17.3(414) | 14.6(366) |
| MEAN NO. OF CORPORA LUTEA/DAM(TOTAL NO.): | 15.7(377) | 16.5(380) | 15.2(350) | 15.5(357) | 17.2(344) | 16.6(415) | 19.0(457) | 17.2(430) |
| FETAL SEX RATIO: MALE:FEMALE | 155:173 | 152:187 | 171:148 | 159:161 | 142:145 | 164:183 | 188:197 | 168:171 |
| % MALE | 47.3 | 44.8 | 53.6 | 49.7 | 49.5 | 47.3 | 48.8 | 49.6 |
| % FEMALE | 52.7 | 55.2 | 46.4 | 50.3 | 50.5 | 52.7 | 51.2 | 50.4 |
| MEAN FETAL BODY WEIGHT (G): | 3.5 | 3.8 | 3.5 | 3.4 | 3.5 | 3.6 | 3.6 | 3.4 |

DATE OF STUDY INITIATION:
DATE OF STUDY TERMINATION:

| | | | | | | | |
|----------|----------|----------|----------|----------|----------|----------|----------|
| 05/24/90 | 07/10/90 | 07/17/90 | 08/29/90 | 12/18/90 | 03/12/91 | 11/26/91 | 12/31/91 |
| 06/17/90 | 08/03/90 | 08/10/90 | 09/21/90 | 01/10/91 | 04/04/91 | 12/18/91 | 01/24/92 |

VEHICLE NO.:

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 1 | 1 | 1 | 5 | 5 | 5 | 2 | 5 | 1 |
|---|---|---|---|---|---|---|---|---|

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NOS. 97-104

| VEHICLE NO. CODE: | 1- CORN OIL | 7- ENVIRONMENTAL CONTROL | 13- 0.2% HYDROXYPROPYLMETHYLCELLULOSE |
|-------------------------|-----------------------------------|--|---------------------------------------|
| 2- 0.5% METHYLCELLULOSE | 8- INTRAVAGINAL SIAM GAVAGE | 14- 0.9% SODIUM CHLORIDE SOLUTION | |
| 3- DEOXYGENATED WATER | 9- INTRAVAGINAL PLACEBO | 15- 0.4% METHYLCELLULOSE | |
| 4- DISTILLED WATER | 10- 1% METHYLCELLULOSE | 16- SPONSOR SUPPLIED CONTROL FORMULATION | |
| 5- DEIONIZED WATER | 11- CORN OIL / 1 % TWEEN 80 | 17- OLIVE OIL | |
| 6- STERILE WATER | 12- 1% POLYVINYL ALCOHOL SOLUTION | 18- CLEAN, FILTERED AIR | |

2
0
8

VIL INDIVIDUAL HISTORICAL CONTROL DATA MATERNAL AND FETAL OBSERVATIONS AT LAPAROMYSTERECTOMY
CHARLES RIVER CD RATS

STUDY NO. 105 106 107 108

NO. OF ANIMALS IN THE CONTROL GROUP: 25 25 25 25
 NO. OF ANIMALS THAT DIED: 0 0 0 0
 NO. OF ANIMALS THAT ABORTED/DELIVERED: 0 0 0 0
 NO. OF ANIMALS EXAMINED AT CESAREAN SECTION: 25 25 25 25
 NO. OF NONGRAVID: 3 3 0 1
 NO. OF GRAVID: 22 22 25 24
 NO. OF DAHS WITH ONLY RESORPTIONS: 0 0 0 0
 NO. OF DAHS WITH LIVE FETUSES: 22 22 25 24
 MEAN NO. VIABLE FETUSES/DAH(TOTAL NO.): 14.7(324) 14.5(318) 14.4(360) 14.2(340)
 MEAN NO. POSTIMPLANTATION LOSSES/DAH(TOTAL NO.): 0.7(16) 1.4(31) 0.8(21) 1.0(23)
 POSTIMPLANTATION LOSS(% PER LITTER): 4.6 8.6 5.4 6.4
 EARLY RESORPTIONS(% PER LITTER): 4.3 8.3 5.4 6.2
 LATE RESORPTIONS(% PER LITTER): 0.3 0.3 0.0 0.2
 DEAD FETUSES(% PER LITTER): 0.0 0.0 0.0 0.0
 MEAN NO. OF IMPLANTATIONS/DAH(TOTAL NO.): 15.5(340) 15.9(349) 15.2(381) 15.1(363)
 MEAN NO. OF CORPORA LUTEA/DAH(TOTAL NO.): 16.9(372) 18.0(396) 17.6(440) 16.4(394)
 FETAL SEX RATIO: MALE:FEMALE 175:149 163:155 190:170 169:171
 % MALE 54.0 51.3 52.8 49.7
 % FEMALE 46.0 48.7 47.2 50.3
 MEAN FETAL BODY WEIGHT (G): 3.5 3.4 3.4 3.5

DATE OF STUDY INITIATION: 02/04/92 05/12/92 08/19/92 05/19/92
 DATE OF STUDY TERMINATION: 02/27/92 06/04/92 09/13/92 06/11/92

VEHICLE NO.: 19 1 4 1

ROUTE OF ADMINISTRATION: ORAL BY GAVAGE- STUDY NOS. 105-108

VEHICLE NO. CODE: 1= CORN OIL 7= ENVIRONMENTAL CONTROL 13= 0.2% HYDROXYPROPYLMETHYLCELLOULOSE
 2= 0.5% METHYLCELLOULOSE 8= INTRAVAGINAL SHAM GAVAGE 14= 0.9% SODIUM CHLORIDE SOLUTION
 3= DEOXYGENATED WATER 9= INTRAVAGINAL PLACEBO 15= 0.4% METHYLCELLOULOSE
 4= DISTILLED WATER 10= 1% METHYLCELLOULOSE 16= SPONSOR SUPPLIED CONTROL FORMULATION
 5= DEIONIZED WATER 11= CORN OIL/ 1% TWEEN 80 17= OLIVE OIL
 6= STERILE WATER 12= 1% POLYVINYL ALCOHOL SOLUTION 18= CLEAN, FILTERED AIR
 19= 0.5% CARBOXYMETHYLCELLOULOSE

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 15

| STUDY NO.: | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|--|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 296/23 | 273/20 | 331/22 | 254/20 | 315/22 | 298/20 | 312/22 | 312/22 |
| AGNATHIA (MANDIBULAR) | 1/1 | 1/1 | | | | | | |
| PERCENT PER LITTER | 0.3 | | | | | | | |
| OMPHALOCELE | | | | | | | | 1/1 |
| PERCENT PER LITTER | | | | | | | | 0.4 |
| NUMBER EXAMINED VISCERALLY | 148/23 | 133/20 | 114/22 | 254/20 | 158/22 | 298/20 | 153/22 | 312/22 |
| ENCEPHALOMENINGOCELE | | | | | 2/1 | | | |
| PERCENT PER LITTER | | | | | 1.3 | | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | | 1/1 |
| PERCENT PER LITTER | | | | | | | | 0.4 |
| NUMBER EXAMINED SKELETALLY | 148/23 | 140/20 | 217/22 | 254/20 | 157/22 | 289/20 | 159/22 | 312/22 |
| VERTEBRAL ANOMALY WITH/WITHOUT RIB ANOMALY | 1/1 | 1/1 | | | | | | 1/1 |
| PERCENT PER LITTER | 0.6 | | | | | | | 0.4 |
| BENT LIMB BONE(S) | | | | | 1/1 | | | |
| PERCENT PER LITTER | | | | | 0.5 | | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | 1/1 | |
| PERCENT PER LITTER | | | | | | | 0.7 | |
| NUMBER WITH EXTERNAL MALFORMATIONS | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 1/1 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 2/1 | 0/0 | 0/0 | 1/1 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 1/1 | 1/1 |
| TOTAL NUMBER WITH MALFORMATIONS | 0/0 | 1/1 | 0/0 | 0/0 | 3/2 | 0/0 | 1/1 | 1/1 |
| PERCENT PER LITTER AFFECTED | 0.0 | 0.3 | 0.0 | 0.0 | 1.8 | 0.0 | 0.7 | 0.4 |

STUDY NO.:

NUMBER EXAMINED EXTERNALLY

| | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|-----|-----|------|----|-----|-----|----|
| AGNATHIA (MANDIBULAR) | | 1/1 | 1/1 | | | | | |
| PERCENT PER LITTER | | 0.4 | 0.4 | | | | | |
| OMPHALOCELE | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.3 | | |
| EXENCEPHALY | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.4 | | | | | |
| MULTIPLE ANOMALIES | | | | 1/1a | | | | |
| PERCENT PER LITTER | | | | 0.3 | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | | | | | | | 1/1 | |
| PERCENT PER LITTER | | | | | | | 0.3 | |

NUMBER EXAMINED VISCERALLY

| | | | | | | | | |
|-----------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| ENCEPHALOMENINGOCELE | 262/21 | 294/22 | 159/24 | 152/23 | 143/22 | 282/20 | 155/23 | 301/22 |
| PERCENT PER LITTER | | | | | | 1/1 | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | 0.3 | |
| PERCENT PER LITTER | | | | | | | | |
| HEART AND/OR GREAT VESSEL ANOMALY | | | | | | 5/1 | | |
| PERCENT PER LITTER | | | | | | 1.9 | | |

NUMBER EXAMINED SKELETALLY

| | | | | | | | | |
|--|--------|--------|--------|--------|--------|--------|--------|--------|
| VERTERAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY | 262/21 | 294/22 | 162/24 | 157/23 | 140/22 | 282/20 | 156/23 | 301/22 |
| PERCENT PER LITTER | | | | 1/1 | | | | 1/1 |
| RIB ANOMALY | | | | 0.6 | | | | 0.3 |
| PERCENT PER LITTER | | | | | | | | |
| BENT LIMB BONE(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNERA(E) MALALIGNED (SEVERE) | | | | | | | 1/1 | |
| PERCENT PER LITTER | | | | | | | 0.4 | |

211

a = MULTIPLE ANOMALIES INCLUDE EXENCEPHALY WITH MYELOSCHISIS, GASTROSCHISIS, ANOPHTHALMIA, VERTERAL ANOMALY, BENT LIMB BONES, ISCHIUH AND PUBIS ABSENT

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITERS)

PAGE 17

| STUDY NO.: | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 0/0 | 1/1 | 2/2 | 1/1 | 0/0 | 1/1 | 1/1 | 0/0 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 6/2 | 0/0 | 0/0 |
| NUMBER WITH SKELETAL MALFORMATIONS | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 1/1 | 0/0 | 1/1 |
| TOTAL NUMBER WITH MALFORMATIONS | 1/1 | 1/1 | 2/2 | 2/2 | 0/0 | 7/3 | 1/1 | 1/1 |
| PERCENT PER LITTER AFFECTED | 0.3 | 0.4 | 0.7 | 1.0 | 0.0 | 2.6 | 0.3 | 0.3 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

| STUDY NO.: | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 360/25 | 303/22 | 370/24 | 338/24 | 403/28 | 385/27 | 378/25 | 316/22 |

| | | | | | | | | |
|---|--|--|-----|--|--|--|--|-----|
| AGNATHIA (MANDIBULAR) | | | 1/1 | | | | | 1/1 |
| PERCENT PER LITTER | | | 0.3 | | | | | 0.3 |
| OMPHALOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MULTIPLE ANOMALIES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

| | | | | | | | | |
|-----------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED VISCERALLY | 174/25 | 147/22 | 178/24 | 164/24 | 403/28 | 194/27 | 191/25 | 110/22 |
| ENCEPHALOMENINGOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HEART AND/OR GREAT VESSEL ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HYDROCEPHALY | | | | | 1/1 | | | |
| PERCENT PER LITTER | | | | | 0.3 | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

STUDY NO.: 17 18 19 20 21 22 23 24

186/25 156/22 192/24 174/24 403/28 191/27 187/25 206/22

NUMBER EXAMINED SKELETALLY
 VERTERRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

PERCENT PER LITTER

RIB ANOMALY

PERCENT PER LITTER

BENT LIMB BONE(S)

PERCENT PER LITTER

COSTAL CARTILAGE ANOMALY

PERCENT PER LITTER

STERNEBRA(E) MALALIGNED (SEVERE)

PERCENT PER LITTER

NUMBER WITH EXTERNAL MALFORMATIONS
 NUMBER WITH VISCERAL MALFORMATIONS
 NUMBER WITH SKELETAL MALFORMATIONS

TOTAL NUMBER WITH MALFORMATIONS

PERCENT PER LITTER AFFECTED

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 | 1/1 |
| 0/0 | 0/0 | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 |
| 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| 0/0 | 0/0 | 1/1 | 0/0 | 1/1 | 0/0 | 0/0 | 1/1 |
| 0.0 | 0.0 | 0.3 | 0.0 | 0.3 | 0.0 | 0.0 | 0.3 |

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

| STUDY NO.: | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 314/20 | 570/41 | 313/23 | 361/24 | 312/22 | 257/20 | 336/22 | 225/16 |
| AGNATHIA (MANDIBULAR) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| OMPHALOCELE | | 1/1 | | | | 1/1 | | |
| PERCENT PER LITTER | | 0.2 | | | | 1.7 | | |
| ELENCEPHALY WITH OR WITHOUT OPEN EYE LID | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MULTIPLE ANOMALIES | | | | | | | | |
| PERCENT PER LITTER | 1/1a | | | | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | 0.3 | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| FETAL ANASARCA | | 1/1 | 1/1 | | | | | 1/1 |
| PERCENT PER LITTER | | 0.2 | 0.3 | | | | | 0.3 |
| GASTROSCHISIS | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.3 | | | | |
| MICROPHthalmia AND/OR ANOPHTHALMIA | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.3 | | | | | |
| CLEFT PALATE | | | | | 1/1b | | | |
| PERCENT PER LITTER | | | | | 0.3 | | | |

a - MULTIPLE ANOMALIES INCLUDE ANASARCA, MICROPHthalmia, ADACTYLY, OMPHALOCELE, TARSAL FLEXURE, TAIL ABSENT WITH ANAL ATRESIA, VERTERRAL AGENESIS, VERTERRAL ANOMALY WITH ASSOCIATED RIB ANOMALY

b - CLASSIFICATION OF CLEFT PALATE FOR THIS FETUS ALSO INCLUDES CLEFT LIP AND NARES ABSENT

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 21

STUDY NO.:

25 26 27 28 29 30 31 32

314/20 285/41 154/23 181/24 151/22 127/20 166/22 115/16

NUMBER EXAMINED VISCERALLY

ENCEPHALOMENINGOCELE

PERCENT PER LITTER

KIDNEY AND/OR URETER ABSENT

PERCENT PER LITTER

HEART AND/OR GREAT VESSEL ANOMALY

PERCENT PER LITTER

HYDROCEPHALY

PERCENT PER LITTER

TESTICULAR HYPOPLASIA

PERCENT PER LITTER

1/1
0.6

1/1
0.3

1/1
0.3

NUMBER EXAMINED SKELETALLY

VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

PERCENT PER LITTER

RIB ANOMALY

PERCENT PER LITTER

BENT LIMB BONE(S)

PERCENT PER LITTER

COSTAL CARTILAGE ANOMALY

PERCENT PER LITTER

STERNEBRA(E) MALALIGNED (SEVERE)

PERCENT PER LITTER

314/20 285/40 159/23 180/24 161/22 130/20 170/22 110/16

1/1
0.6

1/1
0.3

1/1
0.5

2/2
0.7

216

NUMBER WITH EXTERNAL MALFORMATIONS

NUMBER WITH VISCERAL MALFORMATIONS

NUMBER WITH SKELETAL MALFORMATIONS

TOTAL NUMBER WITH MALFORMATIONS

PERCENT PER LITTER AFFECTED

1/1 2/2 1/1 1/1 1/1 1/1 1/1 0/0
 1/1 1/1 0/0 0/0 1/1 0/0 1/1 0/0
 0/0 2/2 0/0 1/1 1/1 1/1 1/1 0/0
 2/2 4/4 1/1 1/1 2/2 2/2 1/1 0/0
 0.6 1.1 0.3 0.3 0.9 2.4 0.3 0.0

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

| STUDY NO.: | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 312/23 | 140/10 | 349/23 | 335/24 | 161/10 | 317/20 | 307/21 | 356/23 |
| AGNATHIA (MANDIBULAR) | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.3 | | | | |
| OMPHALOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MULTIPLE ANOMALIES | | | | | | | 1/1a | |
| PERCENT PER LITTER | | | | | | | 0.3 | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.3 | | |
| FETAL ANASARCA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| GASTROSCHISIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MICROPHthalmia AND/OR ANOPHTHALMIA | | | 2/1 | 1/1 | | | | |
| PERCENT PER LITTER | | | 0.5 | 0.3 | | | | 1/1 |
| CLEFT PALATE | | | | | | | | 0.2 |
| PERCENT PER LITTER | | | | | | | | |
| BRACHYDACTYLY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL AGENESIS | | | | | | | 1/1 | |
| PERCENT PER LITTER | | | | | | | 0.3 | |

217

a - MULTIPLE ANOMALIES INCLUDE VERTEBRAL AGENESIS, MANDIBULAR MICROGNATHIA, DOME-SHAPED HEAD, ANOPHTHALMIA, VERTEBRAL ANOMALY WITH ASSOCIATED RIB ANOMALY

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RAITS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

| STUDY NO.: | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|-----------------------------------|--------|-------|--------|--------|-------|--------|--------|--------|
| NUMBER EXAMINED VISCERALLY | 156/23 | 68/10 | 175/23 | 166/24 | 81/10 | 158/20 | 154/21 | 177/23 |
| ENCEPHALOMENINGOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HEART AND/OR GREAT VESSEL ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HYDROCEPHALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| DIAPHRAGMATIC HERNIA | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.7 | | | | |

NUMBER EXAMINED SKELETALLY
 VERTERAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

| | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|----------------------------------|--------|-------|--------|--------|-------|--------|--------|--------|
| PERCENT PER LITTER | 156/23 | 72/10 | 174/23 | 169/24 | 80/10 | 159/20 | 153/21 | 179/23 |
| RIB ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT LIMB BONE(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNBERA(E) MALALIGNED (SEVERE) | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.5 | | | | |

NUMBER WITH EXTERNAL MALFORMATIONS
 NUMBER WITH VISCERAL MALFORMATIONS
 NUMBER WITH SKELETAL MALFORMATIONS

| | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 1/1 | 0/0 | 2/1 | 2/2 | 0/0 | 1/1 | 1/1 | 1/1 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |

TOTAL NUMBER WITH MALFORMATIONS
 PERCENT PER LITTER AFFECTED

| | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|---------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| TOTAL NUMBER WITH MALFORMATIONS | 1/1 | 0/0 | 3/2 | 3/3 | 0/0 | 1/1 | 1/1 | 1/1 |
| PERCENT PER LITTER AFFECTED | 0.3 | 0.0 | 1.0 | 1.3 | 0.0 | 0.3 | 0.3 | 0.2 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 41 42 43 44 45 46 47 48

NUMBER EXAMINED EXTERNALLY 308/22 369/24 329/23 313/22 308/22 336/24 270/19 307/22
 AGNATHIA (MANDIBULAR) 1/1
 PERCENT PER LITTER 0.4

OMPHALOCELE
 PERCENT PER LITTER
 EXENCEPHALY WITH OR WITHOUT OPEN EYE LID
 PERCENT PER LITTER
 MULTIPLE ANOMALIES
 PERCENT PER LITTER
 TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA
 PERCENT PER LITTER 1/1
 FETAL ANASARCA 0.4
 PERCENT PER LITTER

GASTROSCHISIS
 PERCENT PER LITTER
 MICROPTHALMIA AND/OR ANOPHTHALMIA
 PERCENT PER LITTER 1/1
 CLEFT PALATE 0.3
 PERCENT PER LITTER
 BRACHYDACTYLY
 PERCENT PER LITTER
 VERTEBRAL AGENESIS
 PERCENT PER LITTER

NUMBER EXAMINED VISCERALLY 155/22 183/24 165/23 156/22 154/22 168/24 132/19 156/22
 ENCEPHALOMENINGOCELE
 PERCENT PER LITTER
 KIDNEY AND/OR URETER ABSENT
 PERCENT PER LITTER
 HEART AND/OR GREAT VESSEL ANOMALY
 PERCENT PER LITTER
 HYDROCEPHALY
 PERCENT PER LITTER
 DIAPHRAGMATIC HERNIA
 PERCENT PER LITTER

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

| STUDY NO.: | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 153/22 | 186/24 | 164/23 | 157/22 | 154/22 | 168/24 | 270/19 | 151/22 |

VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

PERCENT PER LITTER

RIB ANOMALY

PERCENT PER LITTER

BENT LIMB BONE(S)

PERCENT PER LITTER

COSTAL CARTILAGE ANOMALY

PERCENT PER LITTER

STERNEBRA(E) MALALIGNED (SEVERE)

PERCENT PER LITTER

NUMBER WITH EXTERNAL MALFORMATIONS

NUMBER WITH VISCERAL MALFORMATIONS

NUMBER WITH SKELETAL MALFORMATIONS

TOTAL NUMBER WITH MALFORMATIONS

PERCENT PER LITTER AFFECTED

| | | | | | | | | |
|------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| TOTAL NUMBER WITH MALFORMATIONS | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 |
| PERCENT PER LITTER AFFECTED | 0.4 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.4 | 0.0 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER CORB CD RATS

| STUDY NO.: | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 |
|---|------------|--------|--------|------------|--------|--------|--------|------------|
| NUMBER EXAMINED EXTERNALLY | 318/24 | 273/21 | 203/14 | 321/22 | 182/15 | 292/20 | 326/23 | 260/20 |
| AGNATHIA (MANDIBULAR) PERCENT PER LITTER | 1/1 0.3 | | | | | | | |
| OMPHALOCELE PERCENT PER LITTER | | | | | | | | 1/1 0.4 |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID PERCENT PER LITTER | 1/1 0.3 | | | | | | | |
| MULTIPLE ANOMALIES PERCENT PER LITTER | | | | 2/2 0.6 | | | | 1/1 0.4 |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA PERCENT PER LITTER | | | | 1/1 0.3 | | | | |
| PETAL ANASARCA PERCENT PER LITTER | | | | | | | | |
| GASTROSCHISIS PERCENT PER LITTER | | | | | | | | |
| MICROPTHALMIA AND/OR ANOPHTHALMIA PERCENT PER LITTER | 1/1 0.3 | | | 1/1 0.3 | | | | |
| CLEFT PALATE PERCENT PER LITTER | | | | | | | | |
| BRACHYDACTYLY PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL AGENESIS PERCENT PER LITTER | | | | | | | | |
| MANDIBULAR MICROGNATHIA PERCENT PER LITTER | | | | | | | | 1/1 0.3 |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

STUDY NO.:

| | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 |
|-----------------------------------|--------|-------|-------|--------|-------|--------|--------|--------|
| NUMBER EXAMINED VISCERALLY | 112/24 | 96/21 | 71/14 | 162/22 | 89/14 | 144/20 | 163/23 | 130/20 |
| ENCEPHALOMENINGOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HEART AND/OR GREAT VESSEL ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HYDROCEPHALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| DIAPHRAGMATIC HERNIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | 1/1 | | |
| LOBULAR AGENESIS OF THE LUNG | | | | | | 0.6 | | |
| PERCENT PER LITTER | | | | | | | | 1/1 |
| | | | | | | | | 1.0 |

NUMBER EXAMINED SKELETALLY
 VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

| | 206/24 | 177/21 | 132/14 | 159/22 | 93/15 | 148/20 | 163/23 | 130/20 |
|------------------------------------|--------|--------|--------|--------|-------|--------|--------|--------|
| PERCENT PER LITTER | | | | | | | | |
| RIB ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT LIMB BONE(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNEBRA(E) MALALIGNED (SEVERE) | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.5 | | | | |
| NUMBER WITH EXTERNAL MALFORMATIONS | 1/1 | 0/0 | 0/0 | 3/2 | 0/0 | 0/0 | 0/0 | 2/2 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 1/1 | 0/0 | 1/1 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 |
| TOTAL NUMBER WITH MALFORMATIONS | 1/1 | 0/0 | 0/0 | 3/2 | 0/0 | 1/1 | 0/0 | 3/2 |
| PERCENT PER LITTER AFFECTED | 0.3 | 0.0 | 0.0 | 1.4 | 0.0 | 0.6 | 0.0 | 1.8 |

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITERS)

| STUDY NO.: | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 355/25 | 315/24 | 311/25 | 299/20 | 364/25 | 268/23 | 313/19 | 349/22 |
| AGNATHIA (MANDIBULAR) | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.3 | | |
| OMPHALOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | | 1/1 | | | | | | |
| PERCENT PER LITTER | | 0.5 | | | | | | |
| MULTIPLE ANOMALIES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.7 | | | | | |
| FETAL ANASARCA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| GASTROSCHISIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MICROPHthalmIA AND/OR ANOPHTHALMIA | | 1/1 | 2/2 | | | | | |
| PERCENT PER LITTER | | 0.5 | 1.3 | | | | 1/1 | 0.3 |
| CLEFT PALATE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BRACHYDACTYLY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL AGENESIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MANDIBULAR MICROGNATHIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | 1/1a | | |
| CYCLOPIA | | | | | | 0.3 | | |
| PERCENT PER LITTER | | | | | | 1/1 | | |
| ASTOMIA | | | | | | 0.3 | | |
| PERCENT PER LITTER | | | | | | | | |
| CRANIORACHISCHISIS | | | 1/1 | | | | | 1/1 |
| PERCENT PER LITTER | | | 0.3 | | | | | 0.3 |
| NUMBER EXAMINED VISCERALLY | 175/25 | 315/24 | 311/25 | 150/20 | 124/25 | 90/22 | 313/19 | 349/22 |
| ENCEPHALOMENINGOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 29

STUDY NO.: 57 58 59 60 61 62 63 64

NUMBER EXAMINED VISCERALLY 175/25 315/24 311/25 150/20 124/25 90/22 313/19 349/22

HEART AND/OR GREAT VESSEL ANOMALY

PERCENT PER LITTER 1/1
 HYDROCEPHALY 0.2
 PERCENT PER LITTER

DIAPHRAGMATIC HERNIA

PERCENT PER LITTER

LOBULAR AGENESIS OF THE LUNG

PERCENT PER LITTER 1/1

RETROPHRAGMATIC AORTIC ARCH

PERCENT PER LITTER 0.2

MALPOSITIONED UTERUS

PERCENT PER LITTER 1/1
 0.8

NUMBER EXAMINED SKELETALLY

VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

PERCENT PER LITTER 180/25 315/24 311/25 149/20 240/25 178/23 313/19 349/22

RIB ANOMALY

PERCENT PER LITTER 1/1
 0.4

BENT LIMB BONE(S)

PERCENT PER LITTER

COSTAL CARTILAGE ANOMALY

PERCENT PER LITTER

STERNERA(E) MALALIGNED (SEVERE)

PERCENT PER LITTER 1/1

VERTEBRAL DYSGENESIS

PERCENT PER LITTER 0.7

INTERRUPTED OSSIFICATION OF THE RIB(S)

PERCENT PER LITTER 1/1
 0.3

NUMBER WITH EXTERNAL MALFORMATIONS

NUMBER WITH VISCERAL MALFORMATIONS

NUMBER WITH SKELETAL MALFORMATIONS

TOTAL NUMBER WITH MALFORMATIONS

PERCENT PER LITTER AFFECTED

| | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 0/0 | 1/1 | 3/3 | 0/0 | 0/0 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 |
| 0/0 | 1/1 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 |
| 0/0 | 2/2 | 4/4 | 1/1 | 0/0 | 2/1 | 2/1 | 2/1 | 2/1 | 2/1 | 2/1 | 2/1 | 2/2 |
| 0.0 | 0.7 | 2.1 | 0.8 | 0.0 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.6 |

VII. INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COB8 CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 30

| STUDY NO. : | 65 | 66 | 67 | 68 | 69 | 70 | 71 | 72 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 328/22 | 327/22 | 289/21 | 311/24 | 356/24 | 303/21 | 298/20 | 298/19 |
| AGNATHIA (MANDIBULAR) | 1/1 | | | | | | | |
| PERCENT PER LITTER | 0.3 | | | | | | | |
| OMPHALOCELE | | 1/1 | | | | | | |
| PERCENT PER LITTER | | 0.3 | | | | | | |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MULTIPLE ANOMALIES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | | | 1/1 | | | | | 1/1 |
| PERCENT PER LITTER | | | 0.3 | | | 1/1 | | 0.3 |
| FETAL ANASARCA | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.3 | | |
| GASTROSCHISIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MICROPTHALMIA AND/OR ANOPHTHALMIA | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.3 | | |
| CLEFT PALATE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BRACHYDACTYLY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL AGENESIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MANDIBULAR MICROGNATHIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| CYCLOPIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| ASTOMIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| CRANIORACHISCHISIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 31

STUDY NO.: 65 66 67 68 69 70 71 72

NUMBER EXAMINED VISCERALLY 328/22 113/22 99/21 311/24 177/24 103/21 103/20 149/19

| | | | | | | | | |
|-----------------------------------|-----|-----|--|--|--|--|--|--|
| ENCEPHALOMENINGOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| KIDNEY AND/OR URETER ABSENT | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HEART AND/OR GREAT VESSEL ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| HYDROCEPHALY | 1/1 | | | | | | | |
| PERCENT PER LITTER | 0.3 | | | | | | | |
| TESTICULAR HYPOPLASIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| DIAPHRAGMATIC HERNIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| LOBULAR AGENESIS OF THE LUNG | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RETROPHAGEAL AORTIC ARCH | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MALPOSITIONED UTERUS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RETINA(S) FOLDED | | 1/1 | | | | | | |
| PERCENT PER LITTER | | 0.9 | | | | | | |

NUMBER EXAMINED SKELETALLY 328/22 214/22 190/21 311/24 179/24 200/21 195/20 149/19

| | | | | | | | | |
|--|--|--|--|--|--|--|--|--|
| VERTERAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT LIMB BONE(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNERA(E) MALALIGNED (SEVERE) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

| | | | | | | | | |
|------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 1/1 | 1/1 | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 1/1 |
| NUMBER WITH VISCERAL MALFORMATIONS | 1/1 | 1/1 | 0/0 | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| TOTAL NUMBER WITH MALFORMATIONS | 2/2 | 2/2 | 1/1 | 0/0 | 0/0 | 2/2 | 0/0 | 1/1 |
| PERCENT PER LITTER AFFECTED | 0.5 | 1.2 | 0.3 | 0.0 | 0.0 | 1.5 | 0.0 | 0.3 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

VII. INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.:

| | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 303/22 | 304/21 | 325/24 | 320/23 | 345/24 | 319/22 | 286/23 | 321/23 |

| | | | | | | | | |
|---|------------|------------|------------|------------|------------|--|------------|------------|
| AGNATHIA (MANDIBULAR) PERCENT PER LITTER | | | | | | | | |
| OPHALOCELE PERCENT PER LITTER | | | | | | | | |
| EXCERPHALY WITH OR WITHOUT OPEN EYE LID PERCENT PER LITTER | | | | | | | | |
| MULTIPLE ANOMALIES PERCENT PER LITTER | | | | | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA PERCENT PER LITTER | 1/1 0.3 | | | | 1/1 0.3 | | 1/1 0.3 | |
| FETAL ANASARCA PERCENT PER LITTER | | | | | | | | |
| GASTROSCHISIS PERCENT PER LITTER | | | | | | | | |
| MICROPTHALMIA AND/OR ANOPHTHALMIA PERCENT PER LITTER | | 1/1 0.3 | | 1/1 0.3 | 1/1 0.2 | | | |
| CLEFT PALATE PERCENT PER LITTER | | | 1/1 0.3 | | | | | |
| BRACHYDACTYLY PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL AGENESIS PERCENT PER LITTER | | | | | | | | |
| MANDIBULAR MICROGNATHIA PERCENT PER LITTER | | | | | | | | |
| CYCLOPIA PERCENT PER LITTER | | | | | | | | |
| ASTOMIA PERCENT PER LITTER | | | | | | | | |
| CRANIORACHISCHISIS PERCENT PER LITTER | | | | | | | | |
| MICROGNATHIA (MAXILLARY) PERCENT PER LITTER | | 1/1 0.3 | | | | | | |
| HYDROCEPHALY WITH OR WITHOUT DOME HEAD PERCENT PER LITTER | | 1/1 0.3 | | | | | 1/1 0.3 | |
| MICROMELIA PERCENT PER LITTER | | | | | | | | 1/1 0.3 |
| UMBILICAL HERNIATION OF INTESTINE PERCENT PER LITTER | | | | | | | | 1/1 0.3 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

VII. INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 73 74 75 76 77 78 79 80

151/22 304/21 325/24 320/23 172/24 162/22 286/23 321/23

NUMBER EXAMINED VISCERALLY
 ENCEPHALOMENINGOCELE
 PERCENT PER LITTER
 KIDNEY AND/OR URETER ABSENT
 PERCENT PER LITTER
 HEART AND/OR GREAT VESSEL ANOMALY
 PERCENT PER LITTER
 HYDROCEPHALY
 PERCENT PER LITTER
 TESTICULAR HYPOPLASIA
 PERCENT PER LITTER
 DIAPHRAGMATIC HERNIA
 PERCENT PER LITTER
 LOBULAR AGENESIS OF THE LUNG
 PERCENT PER LITTER
 RETROESOPHAGEAL AORTIC ARCH
 PERCENT PER LITTER
 MALPOSITIONED UTERUS
 PERCENT PER LITTER
 RETINA(S) FOLDED
 PERCENT PER LITTER
 SITUS INVERSUS
 PERCENT PER LITTER
 STENOTIC CAROTID(S)
 PERCENT PER LITTER

1/1
 0.4
 1/1
 0.3
 1/1
 0.3
 1/1
 0.4

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

| | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| STUDY NO.: | 275/21 | 314/22 | 342/24 | 365/24 | 315/22 | 286/21 | 362/25 | 392/25 |
| NUMBER EXAMINED EXTERNALLY | | | | | | | 1/1 | 0.3 |
| AGNATHIA (MANDIBULAR) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| OMPHALOCELE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MULTIPLE ANOMALIES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | | | | | 1/1 | | | |
| PERCENT PER LITTER | | | | | 0.3 | | | |
| FETAL ANASARCA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| GASTROSCHISIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MICROPHthalmIA AND/OR ANOPHTHALMIA | | | | | | | 2/2 | 0.5 |
| PERCENT PER LITTER | | | | | | | 1/1 | 0.3 |
| CLEFT PALATE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BRACHYDACTYLY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL AGENESIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| MANDIBULAR MICROGNATHIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| CYCLOPIA | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| ASTOMIA | | | | | | | 1/1 | 0.3 |
| PERCENT PER LITTER | | | | | | | | |
| CRANIORACHISCHISIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

STUDY NO.: 81 82 83 84 85 86 87 88

NUMBER EXAMINED EXTERNALLY 275/21 314/22 342/24 365/24 315/22 286/21 362/25 392/25

MICROGNATHIA (MAXILLARY)
 PERCENT PER LITTER
 HYDROCEPHALY WITH OR WITHOUT DOME HEAD
 PERCENT PER LITTER
 MICROMELIA
 PERCENT PER LITTER
 UMBILICAL HERNIATION OF INTESTINE
 PERCENT PER LITTER
 CEBOCEPHALY
 PERCENT PER LITTER
 PINNA(E) - MALPOSITIONED
 PERCENT PER LITTER

1/1
 0.4
 1/1
 0.2
 1/1
 0.3
 1/1
 0.3

NUMBER EXAMINED VISCERALLY
 ENCEPHALOMENINGOCELE
 PERCENT PER LITTER
 KIDNEY AND/OR URETER ABSENT
 PERCENT PER LITTER
 HEART AND/OR GREAT VESSEL ANOMALY
 PERCENT PER LITTER
 HYDROCEPHALY
 PERCENT PER LITTER
 TESTICULAR HYPOPLASIA
 PERCENT PER LITTER
 DIAPHRAGMATIC HERNIA
 PERCENT PER LITTER
 LOBULAR AGENESIS OF THE LUNG
 PERCENT PER LITTER
 RETROESOPHAGEAL AORTIC ARCH
 PERCENT PER LITTER
 MALPOSITIONED UTERUS
 PERCENT PER LITTER
 RETINA(S) FOLDED
 PERCENT PER LITTER
 SITUS INVERSUS
 PERCENT PER LITTER
 STENOTIC CAROTID(S)
 PERCENT PER LITTER

275/21 314/22 342/24 179/24 315/22 140/21 362/25 197/25
 2/2
 0.9
 1/1
 0.4
 1/1
 0.3

STUDY NO.: 81 82 83 84 85 86 87 88

275/21 314/22 342/24 186/24 315/22 146/21 362/25 195/25

NUMBER EXAMINED SKELETALLY

VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

| | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 |
|--|----|----|----|----|----|----|----|----|
| PERCENT PER LITTER | | | | | | | | |
| RIB ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT LIMB BONE(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNEBRA(E) MALALIGNED (SEVERE) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL DYSGENESIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB- HEMISPHERICAL ENLARGEMENT | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| SKULL ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

| | | | | | | | | |
|------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 1/1 | 0/0 | 0/0 | 0/0 | 2/2 | 0/0 | 2/2 | 1/1 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 1/1 | 0/0 | 1/1 | 2/2 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| TOTAL NUMBER WITH MALFORMATIONS | 1/1 | 0/0 | 0/0 | 0/0 | 3/3 | 0/0 | 2/2 | 3/3 |
| PERCENT PER LITTER AFFECTED | 0.4 | 0.0 | 0.0 | 0.0 | 1.1 | 0.0 | 0.5 | 1.2 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

VII. INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 89 90 91 92 93 94 95 96

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25

NUMBER EXAMINED EXTERNALLY

- AGNATHIA (MANDIBULAR)
- PERCENT PER LITTER
- OMPHALOCELE
- PERCENT PER LITTER
- EXENCEPHALY WITH OR WITHOUT OPEN EYE LID
- PERCENT PER LITTER
- MULTIPLE ANOMALIES
- PERCENT PER LITTER
- TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA
- PERCENT PER LITTER
- FETAL ANASARCA
- PERCENT PER LITTER
- GASTROSCHISIS
- PERCENT PER LITTER
- MICROPHthalmIA AND/OR ANOPHTHALMIA
- PERCENT PER LITTER
- CLEFT PALATE
- PERCENT PER LITTER
- BRACHYDACTYLY
- PERCENT PER LITTER
- VERTEBRAL AGENESIS
- PERCENT PER LITTER
- MANDIBULAR MICROGNATHIA
- PERCENT PER LITTER
- CYCLOPIA
- PERCENT PER LITTER
- ASTOMIA
- PERCENT PER LITTER
- CRANIORACHISIS
- PERCENT PER LITTER

1/1 1/1 1/1 1/1 1/1 1/1 1/1
 0.5 0.2 0.2 0.2 0.2 0.2 0.5

1/1
 0.2

233

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 39

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

89 90 91 92 93 94 95 96

STUDY NO.:

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25

NUMBER EXAMINED EXTERNALLY
MICROGNATHIA (MAXILLARY)
PERCENT PER LITTER
HYDROCEPHALY WITH OR WITHOUT DOME HEAD
PERCENT PER LITTER
MICROMELIA
PERCENT PER LITTER
UMBILICAL HERNIATION OF INTESTINE
PERCENT PER LITTER
CEBOCEPHALY
PERCENT PER LITTER
PINNA(E) - MALPOSITIONED
PERCENT PER LITTER

1/1
0.3

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25

NUMBER EXAMINED VISCERALLY
ENCEPHALOMENINGOCELE
PERCENT PER LITTER
KIDNEY AND/OR URETER ABSENT
PERCENT PER LITTER
HEART AND/OR GREAT VESSEL ANOMALY
PERCENT PER LITTER
HYDROCEPHALY
PERCENT PER LITTER
TESTICULAR HYPOPLASIA
PERCENT PER LITTER
DIAPHRAGMATIC HERNIA
PERCENT PER LITTER
LOBULAR AGENESIS OF THE LUNG
PERCENT PER LITTER
RETROPHAGEAL AORTIC ARCH
PERCENT PER LITTER
MALPOSITIONED UTERUS
PERCENT PER LITTER
RETINA(S) FOLDED
PERCENT PER LITTER
SITUS INVERSUS
PERCENT PER LITTER
STENOTIC CAROTID(S)
PERCENT PER LITTER

1/1
0.2

1/1 0.3
1/1 0.3

1/1
0.3

1/1
0.3

234

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

PAGE 40

STUDY NO.:

NUMBER EXAMINED SKELETALLY
 VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

RIB ANOMALY
 PERCENT PER LITTER
 BENT LIMB BONE(S)
 PERCENT PER LITTER
 COSTAL CARTILAGE ANOMALY
 PERCENT PER LITTER

STERNEBRA(E) MALALIGNED (SEVERE)
 PERCENT PER LITTER
 VERTEBRAL DYSGENESIS
 PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE RIB(S)
 PERCENT PER LITTER

RIB- HEMISPHERICAL ENLARGEMENT
 PERCENT PER LITTER

SKULL ANOMALY
 PERCENT PER LITTER

STERNOSCHISIS
 PERCENT PER LITTER

VERTEBRAL AGENESIS
 PERCENT PER LITTER

NUMBER WITH EXTERNAL MALFORMATIONS
 NUMBER WITH VISCERAL MALFORMATIONS
 NUMBER WITH SKELETAL MALFORMATIONS

TOTAL NUMBER WITH MALFORMATIONS
 PERCENT PER LITTER AFFECTED

| | 89 | 90 | 91 | 92 | 93 | 94 | 95 | 96 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 284/21 | 345/24 | 336/21 | 329/22 | 355/23 | 320/21 | 266/20 | 353/25 |
| VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY | 1/1 | | 1/1 | | | | | 1/1 |
| PERCENT PER LITTER | 0.4 | | 0.3 | | | | | 0.3 |
| RIB ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT LIMB BONE(S) | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.4 | | |
| COSTAL CARTILAGE ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNEBRA(E) MALALIGNED (SEVERE) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| VERTEBRAL DYSGENESIS | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB- HEMISPHERICAL ENLARGEMENT | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.3 | | | | | |
| SKULL ANOMALY | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNOSCHISIS | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.3 | | | | | |
| VERTEBRAL AGENESIS | | | | | 1/1 | | | |
| PERCENT PER LITTER | | | | | 0.2 | | | |
| NUMBER WITH EXTERNAL MALFORMATIONS | 2/2 | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 1/1 | 0/0 |
| NUMBER WITH VISCERAL MALFORMATIONS | 0/0 | 1/1 | 0/0 | 1/1 | 1/1 | 0/0 | 0/0 | 2/2 |
| NUMBER WITH SKELETAL MALFORMATIONS | 1/1 | 0/0 | 2/2 | 0/0 | 1/1 | 1/1 | 0/0 | 1/1 |
| TOTAL NUMBER WITH MALFORMATIONS | 3/3 | 2/2 | 2/2 | 1/1 | 2/2 | 1/1 | 1/1 | 3/3 |
| PERCENT PER LITTER AFFECTED | 1.2 | 0.5 | 0.6 | 0.3 | 0.5 | 0.4 | 0.5 | 0.8 |

| 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|--------|--------|--------|--------|--------|--------|--------|--------|
| 328/24 | 339/23 | 319/23 | 320/23 | 287/20 | 347/25 | 385/24 | 339/25 |

2/1
0.7

1/1
0.3

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

| STUDY NO.: | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 328/24 | 339/23 | 319/23 | 320/23 | 287/20 | 347/25 | 385/24 | 339/25 |

MICROGNATHIA (MAXILLARY)
 PERCENT PER LITTER
 HYDROCEPHALY WITH OR WITHOUT DOME HEAD
 PERCENT PER LITTER
 MICROMELIA
 PERCENT PER LITTER
 UMBILICAL HERNIATION OF INTESTINE
 PERCENT PER LITTER
 CEBOCEPHALY
 PERCENT PER LITTER
 PINNA(E) - MALPOSITIONED
 PERCENT PER LITTER
 LOCALIZED FETAL EDEMA
 PERCENT PER LITTER

1/1
 0.3

 1/1
 0.3

1/1
 0.3

NUMBER EXAMINED VISCERALLY
 ENCEPHALOMENINGOCELE
 PERCENT PER LITTER
 KIDNEY AND/OR URETER ABSENT
 PERCENT PER LITTER
 HEART AND/OR GREAT VESSEL ANOMALY
 PERCENT PER LITTER
 HYDROCEPHALY
 PERCENT PER LITTER
 TESTICULAR HYPOPLASIA
 PERCENT PER LITTER
 DIAPHRAGMATIC HERNIA
 PERCENT PER LITTER
 LOBULAR AGENESIS OF THE LUNG
 PERCENT PER LITTER
 RETROESOPHAGEAL AORTIC ARCH
 PERCENT PER LITTER
 MALPOSITIONED UTERUS
 PERCENT PER LITTER

328/24 339/23 319/23 320/23 287/20 347/25 385/24 339/25

 1/1
 0.3

 1/1
 0.3

 1/1
 0.3

 1/1
 0.3

 1/1
 0.3

STUDY NO.: 97 98 99 100 101 102 103 104

328/24 339/23 319/23 320/23 287/20 347/25 385/24 339/25

NUMBER EXAMINED VISCERALLY

RETINA(S) FOLDED
 PERCENT PER LITTER 1/1 1/1
 SITUS INVERSUS
 PERCENT PER LITTER 0.3 0.3
 STENOTIC CAROTID(S)
 PERCENT PER LITTER
 OVARY ABSENT
 PERCENT PER LITTER 1/1
 UTERUS ABSENT
 PERCENT PER LITTER 0.3

328/24 339/23 319/23 320/23 287/20 347/25 385/24 339/25

NUMBER EXAMINED SKELETALLY
 VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

PERCENT PER LITTER
 RIB ANOMALY
 PERCENT PER LITTER
 BENT LIMB BONE(S)
 PERCENT PER LITTER
 COSTAL CARTILAGE ANOMALY
 PERCENT PER LITTER
 STERNEBRA(E) MALALIGNED (SEVERE)
 PERCENT PER LITTER
 VERTEBRAL DYSGENESIS
 PERCENT PER LITTER
 INTERRUPTED OSSIFICATION OF THE RIB(S)
 PERCENT PER LITTER 1/1
 RIB- HEMISPHERICAL ENLARGEMENT
 PERCENT PER LITTER 0.3
 SKULL ANOMALY
 PERCENT PER LITTER
 STERNOSCHISIS
 PERCENT PER LITTER 1/1
 0/4

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITERS)

| STUDY NO.: | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 2/2 | 0/0 | 1/1 | 0/0 | 0/0 | 1/1 | 0/0 | 2/1 |
| NUMBER WITH VISCERAL MALFORMATIONS | 1/1 | 1/1 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 | 1/1 |
| NUMBER WITH SKELETAL MALFORMATIONS | 0/0 | 0/0 | 1/1 | 0/0 | 0/0 | 0/0 | 0/0 | 1/1 |
| TOTAL NUMBER WITH MALFORMATIONS | 2/2 | 1/1 | 3/2 | 0/0 | 0/0 | 1/1 | 0/0 | 4/3 |
| PERCENT PER LITTER AFFECTED | 0.6 | 0.3 | 0.9 | 0.0 | 0.0 | 0.3 | 0.0 | 1.5 |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 105 106 107 108

NUMBER EXAMINED EXTERNALLY 324/22 318/22 360/25 340/24

| | | | | |
|---|-----|--|-----|--|
| AGNATHIA (MANDIBULAR) | | | | |
| PERCENT PER LITTER | | | | |
| OMPHALOCELE | | | | |
| PERCENT PER LITTER | | | | |
| EXENCEPHALY WITH OR WITHOUT OPEN EYE LID | | | | |
| PERCENT PER LITTER | | | | |
| MULTIPLE ANOMALIES | | | | |
| PERCENT PER LITTER | | | | |
| TAIL ANOMALY WITH OR WITHOUT ANAL ATRESIA | 1/1 | | | |
| PERCENT PER LITTER | 0.4 | | | |
| FETAL ANASARCA | | | | |
| PERCENT PER LITTER | | | | |
| GASTROSCHISIS | | | | |
| PERCENT PER LITTER | | | | |
| MICROPHthalmIA AND/OR ANOPHTHALMIA | | | 1/1 | |
| PERCENT PER LITTER | | | 0.4 | |
| CLEFT PALATE | | | | |
| PERCENT PER LITTER | | | | |
| BRACHYDACTYLY | | | | |
| PERCENT PER LITTER | | | | |
| VERTEBRAL AGENESIS | | | | |
| PERCENT PER LITTER | | | | |
| MANDIBULAR MICROGNATHIA | | | | |
| PERCENT PER LITTER | | | | |
| CYCLOPIA | | | | |
| PERCENT PER LITTER | | | | |
| ASTOMIA | | | | |
| PERCENT PER LITTER | | | | |
| CRANIORACHISCHISIS | | | | |
| PERCENT PER LITTER | | | | |

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

STUDY NO.: 105 106 107 108

325/22 318/22 360/25 340/24

NUMBER EXAMINED EXTERNALLY
MICROCYNATHIA (MAXILLARY)
PERCENT PER LITTER
HYDROCEPHALY WITH OR WITHOUT DOME HEAD
PERCENT PER LITTER
MICROMELIA
PERCENT PER LITTER
UMBILICAL HERNIATION OF INTESTINE
PERCENT PER LITTER
CEBOCEPHALY
PERCENT PER LITTER
PINNA(E) - MALPOSITIONED
PERCENT PER LITTER
LOCALIZED FETAL EDEMA
PERCENT PER LITTER

241
NUMBER EXAMINED VISCERALLY
ENCEPHALOMENINGOCELE
PERCENT PER LITTER
KIDNEY AND/OR URETER ABSENT
PERCENT PER LITTER
HEART AND/OR GREAT VESSEL ANOMALY
PERCENT PER LITTER
HYDROCEPHALY
PERCENT PER LITTER
TESTICULAR HYPOPLASIA
PERCENT PER LITTER
DIAPHRAGMATIC HERNIA
PERCENT PER LITTER
LOBULAR AGENESIS OF THE LUNG
PERCENT PER LITTER
RETROESOPHAGEAL AORTIC ARCH
PERCENT PER LITTER
MALPOSITIONED UTERUS
PERCENT PER LITTER

1/1
0.3
1/1
0.3
1/1
0.3

324/22 318/22 360/25 340/24

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF MALFORMATIONS (FETUSES/LITTERS)

STUDY NO.:

105 106 107 108

NUMBER EXAMINED VISCERALLY

324/22 318/22 360/25 340/24

RETINA(S) FOLDED

1/1

PERCENT PER LITTER

0.3

SITUS INVERSUS

1/1

2/2

PERCENT PER LITTER

0.3

0.5

STENOTIC CAROTID(S)

PERCENT PER LITTER

OVARY ABSENT

PERCENT PER LITTER

UTERUS ABSENT

PERCENT PER LITTER

NUMBER EXAMINED SKELETALLY

324/22 318/22 360/25 340/24

VERTEBRAL ANOMALY WITH/WITHOUT ASSOCIATED RIB ANOMALY

1/1

1/1

PERCENT PER LITTER

0.3

0.3

RIB ANOMALY

PERCENT PER LITTER

BENT LIMB BONE(S)

PERCENT PER LITTER

COSTAL CARTILAGE ANOMALY

PERCENT PER LITTER

STERNEBRA(E) MALALIGNED (SEVERE)

PERCENT PER LITTER

VERTEBRAL DYSGENESIS

PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE RIB(S)

PERCENT PER LITTER

RIB- HEMISPHERICAL ENLARGEMENT

PERCENT PER LITTER

SKULL ANOMALY

PERCENT PER LITTER

STERNOSCHISIS

PERCENT PER LITTER

VERTEBRAL AGENESIS

PERCENT PER LITTER

1/1

0.4

INCIDENCE OF MALFORMATIONS (FETUSES/LITERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

| STUDY NO.: | 105 | 106 | 107 | 108 |
|------------------------------------|-----|-----|-----|-----|
| NUMBER WITH EXTERNAL MALFORMATIONS | 1/1 | 1/1 | 0/0 | 0/0 |
| NUMBER WITH VISCERAL MALFORMATIONS | 2/2 | 3/3 | 3/3 | 0/0 |
| NUMBER WITH SKELETAL MALFORMATIONS | 2/2 | 1/1 | 0/0 | 0/0 |
| TOTAL NUMBER WITH MALFORMATIONS | 4/4 | 4/4 | 3/3 | 0/0 |
| PERCENT PER LITTER AFFECTED | 1.3 | 1.3 | 0.8 | 0.0 |

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER CD RATS

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| STUDY NO.: | 296/23 | 273/20 | 331/22 | 254/20 | 315/22 | 298/20 | 312/22 | 312/22 |
| NUMBER EXAMINED EXTERNALLY | | | | 2/2 | 3/3 | | | |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | | | | 0.7 | 0.9 | | | |
| PERCENT PER LITTER | | | | | | | | |
| NUMBER EXAMINED VISCERALLY | 148/23 | 133/20 | 114/22 | 254/20 | 158/22 | 298/20 | 153/22 | 312/22 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 10/7 | 10/6 | 3/3 | | 15/6 | 5.1 | 6/5 | 6/5 |
| PERCENT PER LITTER | 8.5 | 8.4 | 3.2 | | 5.1 | 3.8 | | 1.8 |
| MAJOR BLOOD VESSEL VARIATION | | | 1/1 | 1/1 | | 1/1 | | 1/1 |
| PERCENT PER LITTER | | | 1.5 | 0.5 | | 0.3 | | 0.4 |
| DILATION OF THE ESOPHAGUS | | | 2/2 | | | | | |
| PERCENT PER LITTER | | | 1.8 | | | | | |
| NUMBER EXAMINED SKELETALLY | 148/23 | 140/20 | 217/22 | 254/20 | 157/22 | 298/20 | 159/22 | 312/22 |
| STERNBERA(E) #5 AND/OR #6 UNOSSIFIED | 49/17 | 36/13 | 49/18 | 77/16 | 41/15 | 109/17 | 49/16 | 54/14 |
| PERCENT PER LITTER | 30.6 | 26.1 | 22.9 | 28.5 | 24.5 | 37.5 | 30.2 | 17.2 |
| HYOID UNOSSIFIED | 7/6 | 22/9 | 14/8 | 4/2 | 13/5 | 4/4 | 11/7 | 5/4 |
| PERCENT PER LITTER | 4.1 | 14.3 | 6.5 | 1.3 | 8.1 | 1.4 | 7.4 | 1.7 |
| 14TH RUDIMENTARY RIB(S) | 1/1 | 3/2 | 9/6 | 12/7 | 1/1 | 9/3 | | 19/7 |
| PERCENT PER LITTER | 0.6 | 1.9 | 4.0 | 5.4 | 0.6 | 2.7 | | 5.9 |
| STERNBERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED | 3/3 | | 5/5 | 1/1 | 1/1 | 6/4 | 4/2 | 1/1 |
| PERCENT PER LITTER | 1.9 | | 2.4 | 0.3 | 0.6 | 1.9 | 2.4 | 0.4 |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 5/5 | 9/4 | 1/1 | 1/1 | 1/1 | 5/3 | 1/1 | 2/2 |
| PERCENT PER LITTER | 3.2 | 6.5 | 0.5 | 0.3 | 0.6 | 1.6 | 0.8 | 0.6 |
| STERNBERA(E) MALALIGNED(SLIGHT OR MODERATE) | 2/2 | 2/2 | 5/4 | | | | 6/4 | |
| PERCENT PER LITTER | 1.1 | 1.3 | 2.2 | | | | 3.6 | |
| REDUCED OSSIFICATION OF THE SKULL | | 2/2 | | 2/1 | 10/4 | 1/1 | | 2/2 |
| PERCENT PER LITTER | | 1.7 | | 0.8 | 6.1 | 0.5 | | 0.6 |
| 14TH FULL RIB(S) | 2/1 | 2/1 | | | | | | 1/1 |
| PERCENT PER LITTER | 1.3 | 1.3 | | | | | | 0.3 |

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER CD RATS

STUDY NO.: 1 2 3 4 5 6 7 8

NUMBER EXAMINED SKELETALLY 148/23 140/20 217/22 254/20 157/22 298/20 159/22 312/22

| | | | | | | | |
|---|-----|-----|-----|-----|-----|-----|-----|
| 25 PRESACRAL VERTebrae | 1/1 | | | | | 1/1 | 0.3 |
| PERCENT PER LITTER | 0.8 | | | | | | |
| ENTIRE STERNUM UNOSSIFIED | 1/1 | | | 1/1 | | | |
| PERCENT PER LITTER | 0.6 | | 2/2 | 0.5 | | 1/1 | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | 1.0 | 0.5 | | 0.3 | |
| PERCENT PER LITTER | | | | | | | |
| 27 PRESACRAL VERTebrae | | | | | | | |
| PERCENT PER LITTER | | | | | | 1/1 | |
| 7TH CERVICAL RIB(S) | | | | | | 0.4 | |
| PERCENT PER LITTER | | | | | 3/2 | | |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | 1.7 | | |
| PERCENT PER LITTER | | 1/1 | | | | | |
| PUBIS UNOSSIFIED | | 0.6 | | | | | |
| PERCENT PER LITTER | | | | | | 1/1 | |
| BENT RIB(S) | 1/1 | | 1/1 | 1/1 | | 1/1 | |
| PERCENT PER LITTER | 0.7 | | 0.6 | 0.4 | | 0.4 | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | 1/1 |
| PERCENT PER LITTER | | | | | | | 0.4 |

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 9 10 11 12 13 14 15 16

262/21 294/22 321/24 309/23 283/22 282/20 311/23 301/22

NUMBER EXAMINED EXTERNALLY
 FOCAL SUBCUTANEOUS HEMORRHAGE(S)
 PERCENT PER LITTER

262/21 294/22 159/24 152/23 143/22 282/20 155/23 301/22
 2/2 2/2 4/2 3/3 7/7 5/5 6/5
 0.6 0.7 2.7 2.0 4.7 3.3 1.9

NUMBER EXAMINED VISCERALLY
 RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)
 PERCENT PER LITTER

MAJOR BLOOD VESSEL VARIATION

PERCENT PER LITTER

DILATION OF THE ESOPHAGUS

PERCENT PER LITTER

HEMORRHAGIC KIDNEY(S)

PERCENT PER LITTER

DILATION OF THE BRAIN VENTRICLES

PERCENT PER LITTER

HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY

PERCENT PER LITTER

16/7
 10.7
 9/6
 6.6
 1/1
 0.7

NUMBER EXAMINED SKELETALLY

STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED

PERCENT PER LITTER

HYOID UNOSSIFIED

PERCENT PER LITTER

14TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

STERNEBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE SKULL

PERCENT PER LITTER

14TH FULL RIB(S)

PERCENT PER LITTER

262/21 294/22 162/24 157/23 140/22 282/20 156/23 301/22
 82/21 46/13 29/13 45/17 32/14 67/17 32/12 91/21
 31.7 15.2 18.8 27.1 22.7 24.9 19.0 30.2
 9/8 2/2 5/4 3/3 2/2 1/1 1.0 3/3
 3.4 0.7 2.9 1.9 1.4 0.4 5/5 3/3
 2/2 2/2 1.4 2/2 6/5 6/4 3.3 1.1
 0.7 2/2 2/2 1.2 4.0 2.0 1/1 1/1
 1/1 2/2 0.7 1.2 0.6 0.7 0.5 0.3
 0.3 0.7 5/4 2/2 2/2 3/3 6/5 2.0
 1.2 1.6 1.6 1.7 1.7 1.1 1/1 1/1
 1/1 1/1 1/1 1/1 1/1 5/1 1/1 1/1
 0.3 0.4 0.4 0.6 0.9 1.9 0.5 0.3
 6/4 1/1 1/1 1/1 1/1 1/1 1/1 1/1
 2.5 0.6 0.6 0.6 0.4 0.4 0.4 0.4

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 9 10 11 12 13 14 15 16

262/21 294/22 162/24 157/23 140/22 282/20 156/23 301/22

NUMBER EXAMINED SKELETALLY

25 PRESACRAL VERTERRAE

PERCENT PER LITTER

ENTIRE STERNUM UNOSSIFIED

PERCENT PER LITTER

METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED

PERCENT PER LITTER

27 PRESACRAL VERTERRAE

PERCENT PER LITTER

7TH CERVICAL RIB(S)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES

PERCENT PER LITTER

PUBIS UNOSSIFIED

PERCENT PER LITTER

BENT RIB(S)

PERCENT PER LITTER

GENERAL REDUCED OSSIFICATION OF THE SKELETON

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE PELVIC GIRDLE

PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

1/1
0.6

1/1 1/1
0.3 0.3

1/1 1/1
0.3 0.6

2/2 2/2
0.8 1.2

2/2 1/1
0.8 0.3

3/2 3/1
1.9 2.3

1/1 6/1
0.6 2.3

2/2 1/1
0.7 0.3

1/1
0.3

3/1 6/1
2.3 2.3

1/1 1/1
0.6 0.5

1/1 1/1
1.1 1.1

1/1 1/1
1.1 0.5

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 17 18 19 20 21 22 23 24

NUMBER EXAMINED EXTERNALLY 360/25 303/22 370/24 338/24 403/28 385/27 378/25 316/22

FOCAL SUBCUTANEOUS HEMORRHAGE(S)

NUMBER EXAMINED VISCERALLY 174/25 147/22 178/24 164/24 403/28 194/27 191/25 110/22
 RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) 3/2 2/2 4/4 11/6 10/6 6/5 10/8 12/7
 PERCENT PER LITTER 1.7 3.0 2.2 7.4 2.4 3.0 5.4 14.2
 MAJOR BLOOD VESSEL VARIATION 1/1
 PERCENT PER LITTER 0.3

DILATION OF THE ESOPHAGUS

PERCENT PER LITTER

HEMORRHAGIC KIDNEY(S)

PERCENT PER LITTER

DILATION OF THE BRAIN VENTRICLES

PERCENT PER LITTER

HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY

PERCENT PER LITTER

MISSHAPEN URETER

PERCENT PER LITTER 1/1
 0.5

NUMBER EXAMINED SKELETALLY

STERNBERA(E) #5 AND/OR #6 UNOSSIFIED

PERCENT PER LITTER 186/25 156/22 192/24 174/24 403/28 191/27 187/25 206/22

HYOID UNOSSIFIED

PERCENT PER LITTER 23/15 30/13 28/12 8/6 48/22 27/15 22/9 61/17

14TH RUDIMENTARY RIB(S)

PERCENT PER LITTER 12.6 18.1 14.5 4.4 12.0 16.6 11.6 27.2

STERNBERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED

PERCENT PER LITTER 1/1 3/3 1/1 0.5 2/2 2/2 2/2 25/11

REDUCED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER 0.7 2.0 0.5 0.5 0.5 1.4 35/16 12.0

STERNBERA(E) MALALIGNED(SLIGHT OR MODERATE)

PERCENT PER LITTER 9/6 7/6 15/10 21/10 50/17 39/17 19.1 2/2

REDUCED OSSIFICATION OF THE SKULL

PERCENT PER LITTER 4.6 4.3 7.3 11.6 12.1 20.9 19.1 2/2

14TH FULL RIB(S)

PERCENT PER LITTER 2/2 1/1 1/1 1.4 0.5 1.4 1.1 1.1

PERCENT PER LITTER 2/2 1.2 0.5 1/1 4/4 3/3 7/5 3.2

PERCENT PER LITTER 3/3 1/1 1/1 1/1 1.1 1.7 3/3 1.5

PERCENT PER LITTER 1.4 0.8 0.6 0.5 1.1 1/1 1/1 0.9

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

| | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
|--|----|----|----|----|----|----|----|----|
|--|----|----|----|----|----|----|----|----|

STUDY NO.:

186/25 156/22 192/24 174/24 403/28 191/27 187/25 206/22

NUMBER EXAMINED SKELETALLY

25 PRESACRAL VERTERRAE

PERCENT PER LITTER

ENTIRE STERNUM UNOSSIFIED

PERCENT PER LITTER

METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED

PERCENT PER LITTER

27 PRESACRAL VERTERRAE

PERCENT PER LITTER

7TH CERVICAL RIB(S)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE VERTERRAL ARCHES

PERCENT PER LITTER

PUBIS UNOSSIFIED

PERCENT PER LITTER

BENT RIB(S)

PERCENT PER LITTER

GENERAL REDUCED OSSIFICATION OF THE SKELETON

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE PELVIC GIRDLE

PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

1/1
0.6

2/2 4/2
0.6 3.3

1/1
0.7

2/2 1/1
0.5 0.6
1/1 0.5

1/1
0.6
1/1
0.5

1/1
0.3

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 25 26 27 28 29 30 31 32

NUMBER EXAMINED EXTERNALLY 314/20 570/41 313/23 361/24 312/22 257/20 336/22 225/16

FOCAL SUBCUTANEOUS HEMORRHAGE(S)

314/20 285/41 154/23 181/24 151/22 127/20 166/22 115/16
 3/2 20/14 8/7 12/8 5/3 6/4 3/2 2/2
 1.0 6.7 9.1 6.8 3.0 4.3 1.7 1.8
 2/2
 0.7

NUMBER EXAMINED VISCERALLY
 RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)
 PERCENT PER LITTER
 MAJOR BLOOD VESSEL VARIATION
 PERCENT PER LITTER
 DILATION OF THE ESOPHAGUS
 PERCENT PER LITTER
 HEMORRHAGIC KIDNEY(S)
 PERCENT PER LITTER
 DILATION OF THE BRAIN VENTRICLES
 PERCENT PER LITTER
 HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY
 PERCENT PER LITTER
 MISSHAPEN URETER
 PERCENT PER LITTER

250

NUMBER EXAMINED SKELETALLY
 STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED
 PERCENT PER LITTER
 HYOID UNOSSIFIED
 PERCENT PER LITTER
 14TH RUDIMENTARY RIB(S)
 PERCENT PER LITTER
 STERNEBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED
 PERCENT PER LITTER
 REDUCED OSSIFICATION OF THE 13TH RIB(S)
 PERCENT PER LITTER
 STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)
 PERCENT PER LITTER
 REDUCED OSSIFICATION OF THE SKULL
 PERCENT PER LITTER
 14TH FULL RIB(S)
 PERCENT PER LITTER

314/20 285/40 159/23 180/24 161/22 130/20 170/22 110/16
 39/11 36/16 59/17 17/7 48/17 8/6 22/8 8/4
 11.4 11.8 36.6 9.4 30.0 7.5 12.6 7.1
 2/2 1/1 12/7
 0.7 0.3 7.6
 17/9 11/4 3/2 25/10
 5.3 3.6 1.6 13.3
 1/1 3/2 1/1
 0.2 0.9 0.6
 3/3 4/3 2/2
 1.0 2.6 1.0
 5/5 3/2 6/5 10/9
 1.8 1.9 3.4 6.0
 1/1 2/1 1/1
 0.3 1.2 0.8
 2/1 2/1 1.1

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.:

| | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 314/20 | 285/40 | 159/23 | 180/24 | 161/22 | 130/20 | 170/22 | 110/16 |
| 25 PRESACRAL VERTEBRAE | 1/1 | 1/1 | | | | 1/1 | | 1/1 |
| PERCENT PER LITTER | 0.3 | 0.3 | | | | 0.6 | | 0.8 |

ENTIRE STERNUM UNOSSIFIED

PERCENT PER LITTER

METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED

PERCENT PER LITTER

27 PRESACRAL VERTEBRAE

PERCENT PER LITTER

7TH CERVICAL RIB(S)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES

PERCENT PER LITTER

PUBIS UNOSSIFIED

PERCENT PER LITTER

BENT RIB(S)

PERCENT PER LITTER

GENERAL REDUCED OSSIFICATION OF THE SKELETON

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE PELVIC GIRDLE

PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

2/2
0.6
1/1
0.3

2/2
1.5
1/1
0.6

3/2
1.6

5/2
3.1

1/1
0.4

1/1
0.4

1/1
0.8

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

VIL INDIVIDUAL HISTORICAL CONTROL DATA

CHARLES RIVER COBS CD RATS

33 34 35 36 37 38 39 40

STUDY NO.:

312/23 140/10 349/23 335/24 161/10 317/20 307/21 356/23

NUMBER EXAMINED EXTERNALLY

FOCAL SUBCUTANEOUS HEMORRHAGE(S)

NUMBER EXAMINED VISCERALLY

RENAL PAPTILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)

PERCENT PER LITTER

MAJOR BLOOD VESSEL VARIATION

DILATION OF THE ESOPHAGUS

HEMORRHAGIC KIDNEY(S)

DILATION OF THE BRAIN VENTRICLES

HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY

MISSHAPEN URETER

NUMBER EXAMINED SKELETALLY

STERNERA(E) #5 AND/OR #6 UNOSSIFIED

2 PERCENT PER LITTER

HYOID UNOSSIFIED

PERCENT PER LITTER

14TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

STERNERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

STERNERA(E) MALALIGNED(SLIGHT OR MODERATE)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE SKULL

PERCENT PER LITTER

14TH FULL RIB(S)

PERCENT PER LITTER

PERCENT PER LITTER

156/23 68/10 175/23 166/24 81/10 158/20 154/21 177/23
 5/2 3/3 3/3 3/3 1/1 3/3 4/3 5/4
 2.7 1.8 1.7 1.4 1.4 1.8 2.5 2.7

156/23 72/10 174/23 169/24 80/10 159/20 153/21 179/23
 28/14 21/7 33/15 20/11 8/3 9/7 40/14 31/11
 18.8 28.8 18.2 11.9 9.3 5.5 27.2 18.0
 1/1 1/1 1/1 1/1 0.6 1/1 1/1 3/2
 0.5 6/4 2/2 1/1 13/5 8/5 4/3 4/3
 6/4 9.9 1.2 0.7 15.2 5.4 2.6 2.3
 4.0 4/4 5/3 2/2 1/1 14/9 4/4 13/10
 2.3 8/3 5/3 1.7 1.0 9.3 2.6 8.8
 3/3 11.5 3.0 14/9 4/4 5.2 4/4 2.6
 2.1 6/5 7/5 7.6 5.2 1/1 0.6
 5/5 8.1 4.0 1/1 1/1 1/1 0.6
 3.1 7.6 4.0 5.2 9.3 9.3 2.6

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 58

| STUDY NO.: | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|---|--------|-------|--------|--------|-------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 156/23 | 72/10 | 174/23 | 169/24 | 80/10 | 159/20 | 153/21 | 179/23 |
| 25 PRESACRAL VERTERRAE | 1/1 | | 1/1 | | | | 1/1 | 1/1 |
| PERCENT PER LITTER | 0.6 | | 0.6 | | | | 0.6 | 0.6 |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 27 PRESACRAL VERTERRAE | | 1/1 | | 1/1 | | | 1/1 | |
| PERCENT PER LITTER | | 1.1 | | 1.3 | | | 0.6 | |
| 7TH CERVICAL RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | 1/1 |
| PUBIS UNOSSIFIED | | | | | | | | 0.5 |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | 1/1 | | | 1/1 | 1/1 | 1/1 | 1/1 | 1/1 |
| PERCENT PER LITTER | 0.7 | | | 0.7 | 1.3 | 0.6 | 0.6 | 0.9 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDL | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

| STUDY NO.: | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 308/22 | 369/24 | 329/23 | 313/22 | 308/22 | 336/24 | 270/19 | 307/22 |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | | | | | | | | |
| NUMBER EXAMINED VISCERALLY | 155/22 | 183/24 | 165/23 | 156/22 | 154/22 | 168/24 | 132/19 | 156/22 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | | 2/2 | 6/5 | 4/4 | 1/1 | 2/2 | 1/1 | 5/4 |
| PERCENT PER LITTER | | 1.1 | 3.6 | 2.6 | 0.5 | 1.1 | 0.7 | 3.7 |
| MAJOR BLOOD VESSEL VARIATION | | | | | | | | |
| DILATION OF THE ESOPHAGUS | | | | | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | | | | | |
| MISSHAPEN URETER | | | | | | | | |
| NUMBER EXAMINED SKELETALLY | 153/22 | 186/24 | 164/23 | 157/22 | 154/22 | 168/24 | 270/19 | 151/22 |
| STERNBERA(E) #5 AND/OR #6 UNOSSIFIED | 29/14 | 21/13 | 19/11 | 1/1 | 21/12 | 22/12 | 23/9 | 25/11 |
| PERCENT PER LITTER | 18.3 | 12.2 | 11.3 | 0.6 | 14.0 | 12.6 | 8.0 | 15.4 |
| HYOID UNOSSIFIED | | | | | | | 1/1 | 0.4 |
| PERCENT PER LITTER | 3/3 | 14/9 | 4/3 | 5/3 | | 10/5 | 6/3 | 2/2 |
| 14TH RUDIMENTARY RIB(S) | 1.7 | 8.1 | 2.4 | 3.0 | | 5.5 | 2.2 | 1.2 |
| PERCENT PER LITTER | | | 1/1 | | | 1/1 | | |
| STERNBERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED | | | 0.5 | | | 0.5 | | |
| PERCENT PER LITTER | 4/1 | 1/1 | 4/3 | 1/1 | 4/3 | 4/3 | 3/1 | 7/5 |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 3.0 | 0.6 | 2.4 | 0.8 | 2.5 | 2.4 | 1.4 | 4.2 |
| PERCENT PER LITTER | 6/4 | 5/4 | 8/8 | 14/11 | 9/7 | 14/13 | 19/10 | 3/3 |
| STERNBERA(E) MALALIGNED(SLIGHT OR MODERATE) | 3.6 | 3.5 | 4.4 | 8.5 | 5.5 | 8.3 | 7.1 | 1.9 |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE SKULL | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 14TH FULL RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

**WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS**

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

| STUDY NO.: | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 153/22 | 186/24 | 164/23 | 157/22 | 154/22 | 168/24 | 270/19 | 151/22 |
| 25 PRESACRAL VERTebrae | | | | | | 1/1 | | 6/5 |
| PERCENT PER LITTER | | | | | | 0.5 | | 3.8 |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | 1/1 | 0.4 |
| 27 PRESACRAL VERTebrae | | | | | | | | |
| PERCENT PER LITTER | | 1/1 | | | | 1/1 | | 2/1 |
| 7TH CERVICAL RIB(S) | | 0.5 | | | | 0.7 | | 1.3 |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | | 2/1 | | | | 1/1 | 2/2 | 1/1 |
| PERCENT PER LITTER | | 1.2 | | | | 0.7 | 0.7 | 0.7 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

255

| STUDY NO.: | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 318/24 | 273/21 | 203/14 | 321/22 | 182/15 | 292/20 | 326/23 | 260/20 |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | | | | | | | | |
| NUMBER EXAMINED VISCERALLY | 112/24 | 96/21 | 71/14 | 162/22 | 89/14 | 144/20 | 163/23 | 130/20 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 4/3 | 3/3 | 1/1 | 1/1 | 4/3 | 5/4 | 1/1 | |
| PERCENT PER LITTER | 3.3 | 2.9 | 1.2 | 0.6 | 10.4 | 3.3 | 0.6 | |
| MAJOR BLOOD VESSEL VARIATION | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| DILATION OF THE ESOPHAGUS | | | | | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | | | | | |
| MISSHAPEN URETER | | | | | | | | |
| NUMBER EXAMINED SKELETALLY | 206/24 | 177/21 | 132/14 | 159/22 | 93/15 | 148/20 | 163/23 | 130/20 |
| STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED | 5/4 | 16/8 | 33/11 | 20/10 | 22/9 | 14/7 | 19/12 | 36/13 |
| PERCENT PER LITTER | 2.1 | 8.3 | 25.8 | 12.1 | 24.8 | 9.3 | 11.6 | 28.6 |
| HYOID UNOSSIFIED | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.5 | | | | |
| 14TH RUDIMENTARY RIB(S) | 11/6 | 17/8 | 2/2 | 19/7 | 3/2 | 7/4 | 2/2 | 1/1 |
| PERCENT PER LITTER | 6.7 | 8.3 | 1.4 | 11.9 | 2.5 | 4.6 | 1.3 | 0.6 |
| STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.5 | | | | |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 2/2 | | 2/2 | 3/2 | | | 1/1 | 6/4 |
| PERCENT PER LITTER | 0.8 | | 1.6 | 2.1 | | | 0.6 | 4.2 |
| STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) | 20/14 | 25/16 | 1/1 | 7/7 | | 10/9 | 5/4 | 7/6 |
| PERCENT PER LITTER | 8.9 | 14.1 | 0.8 | 4.0 | | 6.8 | 2.8 | 5.0 |
| REDUCED OSSIFICATION OF THE SKULL | | | | | | | | 2/1 |
| PERCENT PER LITTER | | | | | | | | 1.4 |
| 14TH FULL RIB(S) | | | | | | | | 1/1 |
| PERCENT PER LITTER | | | | | | | | 0.7 |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 62

| STUDY NO.: | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 |
|---|--------|--------|--------|--------|-------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 206/24 | 177/21 | 132/14 | 159/22 | 93/15 | 148/20 | 163/23 | 130/20 |
| 25 PRESACRAL VERTERRAE | 1/1 | | | | | | | |
| PERCENT PER LITTER | 0.7 | | | | | | | |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 27 PRESACRAL VERTERRAE | | | 1/1 | 7/4 | | | | 1/1 |
| PERCENT PER LITTER | | | 0.7 | 4.2 | | | | 0.6 |
| 7TH CERVICAL RIB(S) | | | | | | | 2/2 | |
| PERCENT PER LITTER | | | | | | | 1.2 | |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.7 | | | | | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | | | | 1/1 | | | | 3/2 |
| PERCENT PER LITTER | | | | 0.6 | | | | 2.4 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | | | | | |
| PERCENT PER LITTER | 1/1 | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | 0.5 | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 63

| | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| STUDY NO.: | 355/25 | 315/24 | 311/25 | 299/20 | 364/25 | 268/23 | 313/19 | 349/22 |
| NUMBER EXAMINED EXTERNALLY | | | 1/1 | | | | | |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | | | 0.3 | | | | | |
| TWINNING | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| NUMBER EXAMINED VISCERALLY | 175/25 | 315/24 | 311/25 | 150/20 | 124/25 | 90/22 | 313/19 | 349/22 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 3/2 | | | | 4/3 | | | |
| PERCENT PER LITTER | 1.7 | | | | 2.8 | | | |
| MAJOR BLOOD VESSEL VARIATION | | | | 1/1 | | | | |
| PERCENT PER LITTER | | | | 0.6 | | | | |
| DILATION OF THE ESOPHAGUS | | | | | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | | | | | |
| MISSHAPEN URETER | | | | | | | | |
| NUMBER EXAMINED SKELETALLY | 180/25 | 315/24 | 311/25 | 149/20 | 240/25 | 178/23 | 313/19 | 349/22 |
| STERNBRA(E) #5 AND/OR #6 UNOSSIFIED | 26/14 | 60/18 | 43/12 | 11/7 | 10/6 | 26/11 | 41/10 | 25/12 |
| PERCENT PER LITTER | 14.3 | 19.3 | 14.0 | 7.7 | 3.9 | 14.6 | 13.3 | 7.2 |
| HYOID UNOSSIFIED | | | | | | | | 1/1 |
| PERCENT PER LITTER | | | | | | | | 0.3 |
| 14TH RUDIMENTARY RIB(S) | 4/3 | 8/4 | 17/7 | 6/4 | 22/8 | 16/11 | 70/18 | 37/9 |
| PERCENT PER LITTER | 2.0 | 2.3 | 5.6 | 4.3 | 8.5 | 11.8 | 22.1 | 10.6 |
| STERNBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED | | 1/1 | 1/1 | | | 4/3 | | |
| PERCENT PER LITTER | | 0.5 | 0.3 | | | 3.5 | | |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 5/2 | 4/4 | | 4/3 | | | | 2/2 |
| PERCENT PER LITTER | 2.9 | 1.4 | | 2.6 | | | | 0.5 |
| STERNBRA(E) MALALIGNED(SLIGHT OR MODERATE) | 1/1 | 1/1 | 1/1 | 2/2 | 33/18 | | | 1/1 |
| PERCENT PER LITTER | 0.6 | 0.2 | 0.2 | 1.6 | 13.3 | | | 0.4 |
| REDUCED OSSIFICATION OF THE SKULL | 1/1 | | | | | | | |
| PERCENT PER LITTER | 0.6 | | | | | | | |
| 14TH FULL RIB(S) | | | | 2/1 | | | | 2/1 |
| PERCENT PER LITTER | | | | 0.9 | | | | 0.6 |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

| STUDY NO.: | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 180/25 | 315/24 | 311/25 | 149/20 | 240/25 | 178/23 | 313/19 | 349/22 |
| 25 PRESACRAL VERTEBRAE | 1/1 | | | | | 2/1 | | |
| PERCENT PER LITTER | 0.6 | | | | | 0.9 | | |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | 1/1 | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | 0.5 | | | | | | |
| PERCENT PER LITTER | | | 1/1 | 1/1 | 1/1 | | 1/1 | 1/1 |
| 27 PRESACRAL VERTEBRAE | | | 1.0 | 0.4 | 0.4 | | 0.4 | 0.3 |
| PERCENT PER LITTER | | 3/2 | 2/2 | 1/1 | | | | 5/4 |
| 7TH CERVICAL RIB(S) | | 0.8 | 0.6 | 0.7 | | | | 1.5 |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | 1/1 | 12/5 | 6/3 | | 3/2 | | 2/2 | |
| PERCENT PER LITTER | 0.6 | 3.5 | 2.6 | | 2.0 | | 0.7 | |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 2.2 | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | 1/1 | | | | | | |
| ISCHIUM UNOSSIFIED | | 0.5 | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

259

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 65

STUDY NO.: 65 66 67 68 69 70 71 72

NUMBER EXAMINED EXTERNALLY 328/22 327/22 289/21 311/24 356/24 303/21 298/20 298/19
FOCAL SUBCUTANEOUS HEMORRHAGE(S)
TWINNING

NUMBER EXAMINED VISCERALLY 328/22 113/22 99/21 311/24 177/24 103/21 103/20 149/19
RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)
PERCENT PER LITTER 3/3 1/1 1/1 0.8

MAJOR BLOOD VESSEL VARIATION
DILATION OF THE ESOPHAGUS
HEMORRHAGIC KIDNEY(S)
DILATION OF THE BRAIN VENTRICLES
HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY
MISSHAPEN URETER

NUMBER EXAMINED SKELETALLY 328/22 214/22 190/21 311/24 179/24 200/21 195/20 149/19
STERNERA(E) #5 AND/OR #6 UNOSSIFIED 48/18 34/16 20/13 54/18 17/11 11/7 15/10 26/13
PERCENT PER LITTER 14.7 16.9 10.3 16.6 9.8 6.0 9.2 16.9
HYOID UNOSSIFIED 4/4 1/1
PERCENT PER LITTER 1.2 0.5
14TH RUDIMENTARY RIB(S) 81/17 13/8 3/3 22/9 30/14 7/5 11/7 58/16
PERCENT PER LITTER 24.9 6.0 1.6 7.6 15.1 3.5 4.8 39.3
STERNERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED 2/2 1/1 1/1 1/1 1/1
PERCENT PER LITTER 0.6 0.4 0.3 0.5
REDUCED OSSIFICATION OF THE 13TH RIB(S) 3/2 2/2 1/1 2/2
PERCENT PER LITTER 1.7 0.6 0.5 1.2
STERNERA(E) MALALIGNED(SLIGHT OR MODERATE) 6/4 20/11 4/2 3/3
PERCENT PER LITTER 1.8 6.7 2.6 2.6
REDUCED OSSIFICATION OF THE SKULL
PERCENT PER LITTER
14TH FULL RIB(S) 1/1 1/1
PERCENT PER LITTER 0.5 0.7

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 66

STUDY NO.:

65 66 67 68 69 70 71 72

NUMBER EXAMINED SKELETALLY

328/22 214/22 190/21 311/24 179/24 200/21 195/20 149/19

25 PRESACRAL VERTERRAE

5/2 2/2

PERCENT PER LITTER

2/1

ENTIRE STERNUM UNOSSIFIED

2.4 0.7

PERCENT PER LITTER

0.9

METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED

1/1

PERCENT PER LITTER

1/1

27 PRESACRAL VERTERRAE

0.5

PERCENT PER LITTER

0.7

7TH CERVICAL RIB(S)

4/1 2/2

PERCENT PER LITTER

3/3

REDUCED OSSIFICATION OF THE VERTERRAL ARCHES

1.3 2.9 0.7

PERCENT PER LITTER

1.6

PUBIS UNOSSIFIED

4/3

PERCENT PER LITTER

1/1

BENT RIB(S)

1.4

PERCENT PER LITTER

0.7

GENERAL REDUCED OSSIFICATION OF THE SKELETON

1/1

PERCENT PER LITTER

0.5

REDUCED OSSIFICATION OF THE ISCHIUM

1/1

PERCENT PER LITTER

0.7

REDUCED OSSIFICATION OF THE PELVIC GIRDLE

1/1

PERCENT PER LITTER

0.7

INTERRUPTED OSSIFICATION OF THE 13TH RIB(S)

1/1

PERCENT PER LITTER

0.7

ISCHIUM UNOSSIFIED

1/1

PERCENT PER LITTER

0.7

VIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 67

| STUDY NO. : | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 303/22 | 304/21 | 325/24 | 320/23 | 172/24 | 162/22 | 286/23 | 321/23 |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | | | | | | | | |
| TWINNING | | | | | | | | |
| NUMBER EXAMINED VISCEALLY | 151/22 | 304/21 | 325/24 | 320/23 | 172/24 | 162/22 | 286/23 | 321/23 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 1/1 | 2/1 | 5/3 | 6/3 | | 1/1 | 5/2 | |
| PERCENT PER LITTER | 0.6 | 0.6 | 1.4 | 1.7 | | 0.8 | 5.6 | |
| MAJOR BLOOD VESSEL VARIATION | | | | | | | | |
| DILATION OF THE ESOPHAGUS | | | | | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | | | | | |
| MISSHAPEN URETER | | | | | | | | |
| NUMBER EXAMINED SKELETALLY | 152/22 | 303/21 | 322/24 | 320/23 | 173/24 | 157/22 | 285/23 | 321/23 |
| STERNBERA(E) #5 AND/OR #6 UNOSSIFIED | 6/4 | 16/8 | 29/15 | 31/14 | 18/10 | 8/5 | 31/12 | 36/13 |
| PERCENT PER LITTER | 3.9 | 5.0 | 10.2 | 10.0 | 10.1 | 4.7 | 10.9 | 10.2 |
| HYOID UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | 9/7 | 42/10 | 18/11 | 9/6 | 38/15 | 5/4 | 10/4 | 16/4 |
| 14TH RUDIMENTARY RIB(S) | 5.9 | 14.3 | 5.0 | 2.7 | 22.0 | 3.7 | 3.5 | 5.0 |
| PERCENT PER LITTER | | 1/1 | 3/3 | 2/2 | | | 1/1 | |
| STERNBERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED | | 0.3 | 0.9 | 0.7 | | | 0.3 | |
| PERCENT PER LITTER | 1/1 | | 4/3 | 1/1 | | | 2/2 | 10/6 |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | 0.7 | | 1.2 | 0.3 | | | 0.6 | 3.1 |
| PERCENT PER LITTER | 4/4 | 14/9 | 8/6 | 4/3 | 1/1 | | 5/4 | 5/4 |
| STERNBERA(E) MALALIGNED(SLIGHT OR MODERATE) | | | | | | | | |
| PERCENT PER LITTER | 2.5 | 4.7 | 2.4 | 1.5 | 0.5 | | | 1.8 |
| REDUCED OSSIFICATION OF THE SKULL | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 14TH FULL RIB(S) | | 1/1 | | | | | 1/1 | |
| PERCENT PER LITTER | | 0.3 | | | | | 0.3 | |

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 68

STUDY NO.:

| | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 152/22 | 303/21 | 322/24 | 320/23 | 173/24 | 157/22 | 285/23 | 321/23 |
| 25 PRESACRAL VERTEBRAE | 1/1 | | | | | | | 1/1 |
| PERCENT PER LITTER | 0.6 | | | | | | | 0.3 |
| ENTIRE STERNUM UNOSSIFIED | | | 2/2 | | 1/1 | | | |
| PERCENT PER LITTER | | | 0.6 | | 0.5 | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 27 PRESACRAL VERTEBRAE | | 5/2 | 1/1 | | 4/2 | | | 1/1 |
| PERCENT PER LITTER | | 1.6 | 0.3 | | 2.0 | | | 0.4 |
| 7TH CERVICAL RIB(S) | | | 3/2 | 1/1 | | 5/2 | 1/1 | 1/1 |
| PERCENT PER LITTER | | | 0.9 | 0.3 | | 2.8 | 0.5 | 0.3 |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | 1/1 | 2/1 | | 1/1 | | 1/1 | 1/1 | 4/3 |
| PERCENT PER LITTER | 0.7 | 0.6 | | 0.3 | | 0.7 | 0.5 | 1.4 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE ISCHIUM | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| ISCHIUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB(S) - THICKENED | | | | | 1/1 | | | |
| PERCENT PER LITTER | | | | | 0.5 | | | |
| REDUCED OSSIFICATION OF THE RIB(S) | | | | | | | | 1/1 |
| PERCENT PER LITTER | | | | | | | | 0.4 |

UTIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 69

| STUDY NO.: | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED EXTERNALLY | 275/21 | 314/22 | 342/24 | 365/24 | 315/22 | 286/21 | 362/25 | 392/25 |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) | | | | | | | | |
| TWINNING | | | | | | | | |
| NUMBER EXAMINED VISCERALLY | 275/21 | 314/22 | 342/24 | 179/24 | 315/22 | 140/21 | 362/25 | 197/25 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) | 7/5 | 3/3 | | | | | | |
| PERCENT PER LITTER | 2.7 | 1.0 | | | | | | |
| MAJOR BLOOD VESSEL VARIATION | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| DILATION OF THE ESOPHAGUS | | | | | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | | | | | |
| MISSHAPEN URETER | | | | | | | | |
| HEMORRHAGIC RING AROUND THE IRIS | | 1/1 | | | | | | 1/1 |
| PERCENT PER LITTER | | 0.3 | | | | | | 0.4 |
| NUMBER EXAMINED SKELETALLY | 275/21 | 314/22 | 342/24 | 186/24 | 315/22 | 146/21 | 362/25 | 195/25 |
| STERNBERA(E) #5 AND/OR #6 UNOSSIFIED | 52/12 | 26/12 | 30/12 | 8/6 | 15/5 | 7/5 | 72/20 | 8/5 |
| PERCENT PER LITTER | 17.8 | 8.3 | 8.7 | 4.1 | 5.0 | 5.3 | 19.9 | 3.8 |
| HYOID UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 14TH RUDIMENTARY RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNBERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| STERNBERA(E) MALALIGNED(SLIGHT OR MODERATE) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE SKULL | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 14TH FULL RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 70

STUDY NO.:

275/21 314/22 342/24 186/24 146/21 362/25 195/25
 1/1 1/1 1/1 0.2
 0.3 1/1 0.3

81 82 83 84 85 86 87 88

NUMBER EXAMINED SKELETALLY

25 PRESACRAL VERTEBRAE

PERCENT PER LITTER

ENTIRE STERNUM UNOSSIFIED

PERCENT PER LITTER

METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED

PERCENT PER LITTER

27 PRESACRAL VERTEBRAE

PERCENT PER LITTER

7TH CERVICAL RIB(S)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES

PERCENT PER LITTER

PUBIS UNOSSIFIED

PERCENT PER LITTER

BENT RIB(S)

PERCENT PER LITTER

GENERAL REDUCED OSSIFICATION OF THE SKELETON

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE ISCHIUM

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE PELVIC GIRDLE

PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

ISCHIUM UNOSSIFIED

PERCENT PER LITTER

RIB(S) - THICKENED

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE RIB(S)

PERCENT PER LITTER

265

1/1 6/4 1/1 1/1
 0.3 1.7 0.3 0.3
 2/1 2/2 4/4 1/1
 0.7 0.6 1.3 0.3
 2/2 0.5
 4/4 2/2
 1.3 0.5
 1/1 0.7
 1/1 0.3
 2/2 0.5
 2/2 0.5
 1/1 0.3
 1/1 0.3

1/1
0.4

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 71

| STUDY NO.: | 89 | 90 | 91 | 92 | 93 | 94 | 95 | 96 |
|---|-------------|-------------|--------------|-------------|--------------|--------------|---------------|--------------|
| NUMBER EXAMINED EXTERNALLY | 284/21 | 345/24 | 336/21 | 329/22 | 355/23 | 320/21 | 266/20 | 353/25 |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) TWINNING | | | | | | | | |
| NUMBER EXAMINED VISCERALLY | 284/21 | 345/24 | 336/21 | 329/22 | 355/23 | 320/21 | 266/20 | 353/25 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) PERCENT PER LITTER | 1/1 0.4 | 1/1 0.3 | | | | 1/1 0.3 | 1/1 0.4 | |
| MAJOR BLOOD VESSEL VARIATION PERCENT PER LITTER | | | 1/1 0.3 | | | | | 1/1 0.3 |
| DILATION OF THE ESOPHAGUS | | | | | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | | | | | |
| MISSHAPEN URETER | | | | | | | | |
| HEMORRHAGIC RING AROUND THE IRIS PERCENT PER LITTER | | | | | | | | |
| NUMBER EXAMINED SKELETALLY | 284/21 | 345/24 | 336/21 | 329/22 | 355/23 | 320/21 | 266/20 | 353/25 |
| STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED PERCENT PER LITTER | 18/7 6.0 | 26/9 7.0 | 12/9 3.5 | 17/9 4.8 | 15/6 4.1 | 23/10 7.3 | 30/14 12.3 | 30/11 8.5 |
| HYOID UNOSSIFIED PERCENT PER LITTER | | | | | 5/4 1.4 | | | 1/1 0.3 |
| 14TH RUDIMENTARY RIB(S) PERCENT PER LITTER | 5/3 1.7 | 7/6 1.9 | 31/11 8.4 | 3/2 1.0 | 22/12 6.2 | 28/11 8.2 | 6/3 1.9 | 8/6 2.4 |
| STERNEBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED PERCENT PER LITTER | | | | 1/1 0.3 | | 1/1 0.3 | 0.4 | |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) PERCENT PER LITTER | 6/5 2.1 | 2/2 0.6 | 2/1 0.5 | 9/7 3.1 | 2/2 0.6 | | 4/4 1.4 | 9/6 2.4 |
| STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) PERCENT PER LITTER | 2/2 0.7 | 2/2 0.6 | | 2/2 0.6 | | 5/3 1.7 | 7/5 2.4 | 3/2 0.8 |
| REDUCED OSSIFICATION OF THE SKULL PERCENT PER LITTER | | | | | | | | |
| 14TH FULL RIB(S) PERCENT PER LITTER | | | | | | | | |
| 25 PRESACRAL VERTebrae PERCENT PER LITTER | | 1/1 0.2 | | | | | 1/1 0.3 | |

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 72

STUDY NO.:

89 90 91 92 93 94 95 96

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25

NUMBER EXAMINED SKELETALLY
 ENTIRE STERNUM UNOSSIFIED

PERCENT PER LITTER

METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED

PERCENT PER LITTER

27 PRESACRAL VERTEBRAE

PERCENT PER LITTER

7TH CERVICAL RIB(S)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES

PERCENT PER LITTER

PUBIS UNOSSIFIED

PERCENT PER LITTER

BENT RIB(S)

PERCENT PER LITTER

GENERAL REDUCED OSSIFICATION OF THE SKELETON

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE ISCHIUM

PERCENT PER LITTER/A

REDUCED OSSIFICATION OF THE PELVIC GIRDLE

PERCENT PER LITTER

INTERRUPTED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

ISCHIUM UNOSSIFIED

PERCENT PER LITTER

RIB(S) - THICKENED

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE RIB(S)

PERCENT PER LITTER

CENTRA UNOSSIFIED

PERCENT PER LITTER

CERVICAL CENTRUM #1 OSSIFIED

PERCENT PER LITTER

14TH RUDIMENTARY RIB(S) WITH 15TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 73

STUDY NO.:

97 98 99 100 101 102 103 104

NUMBER EXAMINED EXTERNALLY

328/24 339/23 319/23 320/23 287/20 347/25 385/24 339/25

FOCAL SUBCUTANEOUS HEMORRHAGE(S)

TWINNING

NUMBER EXAMINED VISCERALLY

328/24 339/24 319/23 320/23 287/20 347/25 385/24 339/25

RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)

PERCENT PER LITTER

1/1

MAJOR BLOOD VESSEL VARIATION

PERCENT PER LITTER

0.3

DILATION OF THE ESOPHAGUS

HEMORRHAGIC KIDNEY(S)

DILATION OF THE BRAIN VENTRICLES

HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY

MISSHAPENED URETER

HEMORRHAGIC RING AROUND THE IRIS

PERCENT PER LITTER

1/1

THYRUS HEMORRHAGIC

PERCENT PER LITTER

0.3

BRAIN HEMORRHAGE

PERCENT PER LITTER

0.3

NUMBER EXAMINED SKELETALLY

STERNERA(E) #5 AND/OR #6 UNOSSIFIED

PERCENT PER LITTER

328/24 339/24 319/23 320/23 287/20 347/24 385/24 339/25
 34/14 23/13 32/11 27/10 12/6 14/7 12/7 37/13
 9.6 6.6 9.0 8.5 4.1 3.7 3.1 11.2

HYOID UNOSSIFIED

PERCENT PER LITTER

1/1

14TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

13/10 19/9 8/7 3/3 15/8 2/2 14/7 5/5

STERNERA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED

PERCENT PER LITTER

4.5 5.6 2.7 1.0 5.2 0.5 3.7 1.7

REDUCED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

1/1 2/2 0.6 0.3 2/2 16/9 8/3 11/7

STERNERA(E) MALALIGNED(SLIGHT OR MODERATE)

PERCENT PER LITTER

0.3 4/3 2/1 0.5 2/2 0.7 4.1 2.4

REDUCED OSSIFICATION OF THE SKULL

PERCENT PER LITTER

1/1 1/1 1/1 0.3 0.3

PERCENT PER LITTER

1/1 1/1 1/1 0.3 0.3

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.:

| | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 328/24 | 339/24 | 319/23 | 320/23 | 287/20 | 347/24 | 385/24 | 339/25 |
| 14TH FULL RIB(S) | 1/1 | | | | | 1/1 | | |
| PERCENT PER LITTER | 0.5 | | | | | 0.3 | | |
| 25 PRESACRAL VERTERRAE | | | 3/1 | 1/1 | | | | |
| PERCENT PER LITTER | | | 0.9 | 0.3 | | | | |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 27 PRESACRAL VERTERRAE | 1/1 | | 1/1 | | | | | |
| PERCENT PER LITTER | 0.5 | | 0.3 | | | | | |
| 7TH CERVICAL RIB(S) | 1/1 | | 3/3 | 1/1 | 1/1 | 4/2 | 2/2 | 2/2 |
| PERCENT PER LITTER | 0.3 | | 0.9 | 0.3 | 0.4 | 1.1 | 0.5 | 0.5 |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | | 2/2 | 2/2 | |
| PERCENT PER LITTER | | | | | | 0.5 | 0.6 | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | 3/2 | 4/2 | | | 12/4 | | 1/1 | 2/2 |
| PERCENT PER LITTER | 1.1 | 1.2 | | | 4.4 | | 0.3 | 0.5 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.3 | | | | | |
| REDUCED OSSIFICATION OF THE ISCHIUM | | | | | | | | |
| PERCENT PER LITTER(A) | | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| ISCHIUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB(S) - THICKENED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 75

| STUDY NO.: | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|--|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 328/24 | 339/24 | 319/23 | 320/23 | 287/20 | 347/24 | 385/24 | 339/25 |
| REDUCED OSSIFICATION OF THE RIB(S) | 1/1 | | | | 2/2 | | | |
| PERCENT PER LITTER | 0.3 | | | | 0.7 | | | |
| CENTRA UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| CERVICAL CENTRUM #1 OSSIFIED | | | | | 48/16 | 66/16 | 50/18 | 67/17 |
| PERCENT PER LITTER | | | | | 16.1 | 17.8 | 13.3 | 20.3 |
| 14TH RUDIMENTARY RIB(S) WITH 15TH RUDIMENTARY RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| UNCO-OSSIFIED VERTEBRAL CENTRA | | | | | | 1/1 | | |
| PERCENT PER LITTER | | | | | | 0.3 | | |

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

STUDY NO.: 105 106 107 108

324/22 318/22 360/25 340/24

NUMBER EXAMINED EXTERNALLY
 FOCAL SUBCUTANEOUS HEMORRHAGE(S)
 TWINNING

324/22 318/22 360/25 340/24
 1/1
 0.3

NUMBER EXAMINED VISCERALLY
 RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)
 PERCENT PER LITTER

MAJOR BLOOD VESSEL VARIATION
 PERCENT PER LITTER

DILATION OF THE ESOPHAGUS
 HEMORRHAGIC KIDNEY(S)

DILATION OF THE BRAIN VENTRICLES
 HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY

MISSHAPENED URETER
 HEMORRHAGIC RING AROUND THE IRIS

PERCENT PER LITTER
 THYMUS HEMORRHAGIC

PERCENT PER LITTER
 BRAIN HEMORRHAGE

PERCENT PER LITTER
 KIDNEY- CYST(S)

PERCENT PER LITTER

1/1
 0.4

NUMBER EXAMINED SKELETALLY
 STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED

PERCENT PER LITTER

HYOID UNOSSIFIED
 PERCENT PER LITTER

14TH RUDIMENTARY RIB(S)
 PERCENT PER LITTER

STERNEBRA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED
 PERCENT PER LITTER

REDUCED OSSIFICATION OF THE 13TH RIB(S)
 PERCENT PER LITTER

STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)
 PERCENT PER LITTER

324/22 318/22 360/25 340/24
 54/16 31/12 24/10 19/8
 16.8 9.9 6.5 5.1

1/1
 0.3
 9/8 5/3 5/3 4/4
 2.5 1.6 1.3 1.2
 1/1 1/1 1/1

0.4 0.3
 10/5 9/6 6/5 11/5
 3.2 2.9 1.6 2.9

2/2
 0.5

VIL INDIVIDUAL HISTORICAL CONTROL DATA INCIDENCE OF VARIATIONS (FETUSES/LITTERS)
 CHARLES RIVER COBS CD RATS

| STUDY NO.: | 105 | 106 | 107 | 108 |
|---|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 324/22 | 318/22 | 360/25 | 340/24 |
| REDUCED OSSIFICATION OF THE SKULL | | | | |
| PERCENT PER LITTER | | | | |
| 14TH FULL RIB(S) | | | 1/1 | 6/1 |
| PERCENT PER LITTER | | | 0.3 | 1.6 |
| 25 PRESACRAL VERTEBRAE | | | | |
| PERCENT PER LITTER | | | | |
| ENTIRE STERNUM UNOSSIFIED | | | | |
| PERCENT PER LITTER | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | |
| PERCENT PER LITTER | | 1/1 | | |
| 27 PRESACRAL VERTEBRAE | | 0.3 | | |
| PERCENT PER LITTER | | 3/2 | 5/5 | 7/5 |
| 7TH CERVICAL RIB(S) | 5/4 | 1.0 | 1.3 | 2.3 |
| PERCENT PER LITTER | 1.4 | | | 1/1 |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | 0.3 |
| PERCENT PER LITTER | | | | |
| PUBIS UNOSSIFIED | | | | |
| PERCENT PER LITTER | | 2/2 | 5/4 | 3/2 |
| BENT RIB(S) | 5/3 | 0.7 | 1.5 | 0.8 |
| PERCENT PER LITTER | 1.5 | | | |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | |
| PERCENT PER LITTER | | | | |
| REDUCED OSSIFICATION OF THE ISCHIUM | | | | |
| PERCENT PER LITTER(A) | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | |
| PERCENT PER LITTER | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | |
| PERCENT PER LITTER | | | | |
| ISCHIUM UNOSSIFIED | | | | |
| PERCENT PER LITTER | | | | |
| RIB(S) - THICKENED | | | | |
| PERCENT PER LITTER | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

| STUDY NO.: | 105 | 106 | 107 | 108 |
|--|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 324/22 | 318/22 | 360/25 | 340/24 |
| REDUCED OSSIFICATION OF THE RIB(S) | 1/1 | 1/1 | 1/1 | |
| PERCENT PER LITTER | 0.3 | 0.3 | 0.5 | |
| CENTRA UNOSSIFIED | | | | |
| PERCENT PER LITTER | | | | |
| CERVICAL CENTRUM #1 OSSIFIED | 49/15 | 46/14 | 48/16 | 50/17 |
| PERCENT PER LITTER | 15.8 | 14.5 | 13.7 | 14.3 |
| 14TH RUDIMENTARY RIB(S) WITH 15TH RUDIMENTARY RIB(S) | | | | |
| PERCENT PER LITTER | | | | |
| UNCO-OSSIFIED VERTEBRAL CENTRA | | | | |
| PERCENT PER LITTER | | | | |

WIL-15218
Velsicol Chemical Corporation

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

APPENDIX D

Study Protocol



Study Number: WIL-15218

PROTOCOL AMENDMENT II

Sponsor: Velsicol Chemical Corporation

A. Title of Study:

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

B. Protocol Modification:

1) II. PERSONNEL INVOLVED IN THE STUDY

B. WIL Study Director

John Knapp, B.S.
Manager, Developmental, Reproductive
and Neurotoxicology

C. Reason for Protocol Modification:

- 1) Due to the resignation of Dr. Lamb, a new Study Director has been assigned.

Approved By:

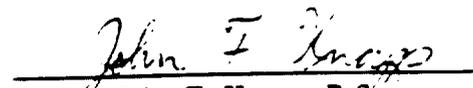
Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-5119


John M. Bergman
Manager, Regulatory Affairs

9/12/94
Date

Prepared By:

WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281


John F. Knapp, B.S.
Study Director

9-2-94
Date



Study Number: WIL-15218

PROTOCOL AMENDMENT I

Sponsor: Velsicol Chemical Corporation

A. Title of Study:

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

B. Protocol Modification:

1) VII. EXPERIMENTAL DESIGN

E. Method, Frequency and Analysis of Test Material Preparations

2. Frequency of Preparation

Suspensions of the test material will be prepared fresh weekly prior to dosing and stored refrigerated.

3. Analysis of Dosing Preparations for Test Material Concentration

Each batch of test material prepared for administration will be prepared according to the protocol and analyzed prior to dosing.

C. Reason for Protocol Modification:

- 1) To document that dosing formulations will be prepared and analyzed prior to dosing, rather than on the day prior to dosing. This change in the protocol design was made to allow flexibility in the schedule for the preparation and analysis of dosing formulations for this study.

Approved By:

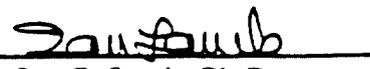
Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-5119


John M. Bergman
Manager, Regulatory Affairs

8/15/94
Date

Prepared By:

WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281


Ian C. Lamb, Ph.D.
Study Director

8-11-94
Date



PROTOCOL

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

(EPA TSCA Guidelines)

Study No.: WIL-15218

For:

Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-3713

By

WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281

August 4, 1994

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

WIL Project No.: WIL-15218

I. OBJECTIVE OF STUDY

To determine the potential of the test material to induce developmental toxicity in rats.

II. PERSONNEL INVOLVED IN THE STUDY

A. Sponsor Representative

John M. Bergman
Manager
Regulatory Affairs

B. WIL Study Director

Ian C. Lamb, Ph.D.
Senior Toxicologist, Developmental, Reproductive
and Neurotoxicology

C. Study Responsibilities

1. Joseph F. Holson, Ph.D.
President, Director
2. Mark D. Nemecek, B.S.
Associate Director of Developmental
and Reproductive Toxicology
3. Lisa Simon, M.B.A., B.S., M.T.(ASCP)
Supervisor of Clinical Pathology
4. Stanley E. Kopp
Systems Manager
5. Sally Keets, A.S.
Manager of In-Life Facilities
6. John Knapp, B.S.
Manager, Developmental, Reproductive
and Neurotoxicology
7. Kevin Oberholtzer, B.S.
Manager of Technical Report Writing
8. Deborah L. Little
Manager of Quality Assurance

II. PERSONNEL INVOLVED IN THE STUDY (continued)

9. Loren Severs, M.S.
Manager of Analytical Chemistry
10. Ian C. Lamb, Ph.D.
Manager of Pharmacy
11. Kerin Clevidence, B.S.
Acting Section Head I - Pathology and
Developmental Toxicology Laboratory
12. Robert Dahlgren, D.V.M., Ph.D., Diplomate A.C.V.P.
Director of Pathology

III. STUDY SCHEDULE DATA

- A. Proposed Experimental Start Date: August, 1994
- B. Proposed Experimental Termination Date: (In-Life Study) October, 1994
- C. Proposed Report Date: January, 1995

IV. TEST ARTICLE DATA

- A. Identification: Isodecyl Benzoate
- B. Lot Number: C5-8
- C. Purity: Approximately 98% mixed C_{9,11} isomers, but assume 100% for dose calculations.
- D. Stability: The test material is considered stable when stored as described below.
- E. Physical Description: Clear, colorless liquid.
- F. Storage Conditions: Room Temperature.
- G. Reserve Samples: Reserve 1 gram samples of the test article will be taken in accordance with standard operating procedures and stored in the Archives at WIL Research Laboratories, Inc.
- H. Personnel Safety Data: See attached MSDS.

A Developmental Toxicity Study in Rats

V. TEST SYSTEM

- A. Species: Rat
- B. Strain: Sprague-Dawley CrI:CD®BR
- C. Source: The Charles River Breeding Laboratories, Inc.
9801 Shaver Road
Portage, Michigan 49081
- D. Number on Study: 100 females (minimum of 120 purchased).
- E. Body Weight Range: Minimum of 220g at initiation of breeding
- F. Approximate Age: 80 to 120 days at initiation of breeding
- G. Identification System: Each animal will be uniquely identified by a Monel® metal ear-tag displaying the animal number. Individual cage cards will be affixed to each cage and will display the animal number, group number, study number, dosage level, sex and the date of animal arrival.
- H. Justification for Selection: This species and strain of animal have been recognized as appropriate for developmental toxicity studies. WIL Research Laboratories, Inc., has historical data on the background incidence of fetal malformations and developmental variations in this species from this same strain and source. This animal model has been proven susceptible to the effects of positive teratogenic agents.

VI. SPECIFIC MAINTENANCE SCHEDULE

A. Animal Housing

The animals will be individually housed (except during mating) in suspended wire-mesh cages in an environmentally controlled room during the study. Nesting material will not be provided as euthanization is scheduled prior to anticipated parturition. Animals selected for study will be housed in clean cages elevated above cage-board or other suitable material that will be changed at least three times each week.

B. Environmental Conditions

Controls will be set to maintain temperature at $72^{\circ} \pm 3^{\circ}\text{F}$ and relative humidity at 40-80%. Air handling units will be set to provide approximately 10 fresh air changes per hour. Fluorescent lighting controlled by light timers will provide illumination for a 12-hour light/dark photoperiod. Temperature and relative humidity will be recorded once daily.

VI. SPECIFIC MAINTENANCE SCHEDULE

C. Drinking Water

Tap water will be available *ad libitum*. Filters servicing the automatic watering system are changed regularly according to Standard Operating Procedures. Water supplying the laboratory is analyzed for contaminants according to WIL Standard Operating Procedures.

D. Basal Diet

Purina® Certified Rodent Chow® #5002 will be offered *ad libitum* during the study. Periodic analyses of the certified feed for the presence of heavy metals and pesticides is performed and provided by the manufacturer.

VII. EXPERIMENTAL DESIGN

A. Animal Receipt and Quarantine

Each animal will be inspected by a qualified technician upon receipt. Rats judged to be in good health and suitable as test animals will be immediately placed in quarantine for a minimum of 7 to 10 days. All rats will be initially weighed and permanently identified with an ear-tag. During the quarantine period each rat will be observed twice daily for changes in general appearance and behavior. Prior to randomization, those animals judged to be suitable test subjects will be identified.

B. Randomization

At the conclusion of the quarantine period, animals judged to be suitable test subjects and meeting acceptable body weight requirements, will be cohabitated with a male. Females for which there is evidence of mating will be consecutively assigned in a block design to one control group and three test article groups of 25 rats each.

C. Breeding Procedure

A female will be cohabitated with a male rat of the same strain and source in a suspended wire-mesh cage for mating. Detection of mating will be confirmed by evidence of a copulatory plug or by a vaginal smear for sperm. Confirmation of mating will result in the female being returned to an individual suspended wire-mesh cage (assigned to a group) and the day designated as day "0" of gestation.

VII. EXPERIMENTAL DESIGN (continued)

D. Organization of Test Groups, Dosage Levels and Treatment Regimen

1. Organization of Test Groups

The dosage levels will be determined from an exploratory range-finding study (WIL Study No. 15217) and will be provided by the Sponsor Representative after consultation with the WIL Study Director. The following diagram presents the study group arrangement.

| <u>Group Number</u> | <u>Group Name</u> | <u>Test Substance</u> | <u>Dosage Level (mg/kg/day)</u> | <u>Dosage Concentration (mg/ml)</u> | <u>Dosage Volume (ml/kg)</u> | <u>Number of Females</u> |
|---------------------|-------------------|-----------------------|---------------------------------|-------------------------------------|------------------------------|--------------------------|
| 1 | Vehicle Control | Mazola® Corn Oil | 0 | 0 | 5 | 25 |
| 2 | Low Dose | Isodecyl Benzoate | 30 | 6 | 5 | 25 |
| 3 | Mid Dose | Isodecyl Benzoate | 300 | 60 | 5 | 25 |
| 4 | High Dose | Isodecyl Benzoate | 1000 | 200 | 5 | 25 |

2. Control Material

Mazola® Corn Oil

3. Route and Rationale of Test Material Administration

The route of administration will be oral since this is the anticipated route of exposure for the general population. Historically, this route has been used extensively for studies of this nature. The dosing cannulas for oral administration by gavage will be constructed of 16-gauge stainless-steel (Popper and Sons, Inc., New Hyde Park, New York).

4. Treatment Regimen

The test and control materials will be administered as a single daily dose during the period of major organogenesis, gestation days 6 through 15. All animals will be dosed at approximately the same time each day.

5. Adjustment of Dosages

Individual dosages will be calculated based on the most recent body weight to provide the proper mg/kg/day dosage.

VIL INDIVIDUAL HISTORICAL CONTROL DATA

CHARLES RIVER COBS CD RATS

STUDY NO.: 89 90 91 92 93 94 95 96

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25

NUMBER EXAMINED EXTERNALLY
 FOCAL SUBCUTANEOUS HEMORRHAGE(S)
 TWINNING

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25
 1/1 1/1 1/1 1/1 1/1 1/1 1/1
 0.4 0.3 1/1 0.3 0.4 1/1 0.3

NUMBER EXAMINED VISCERALLY
 RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)
 PERCENT PER LITTER
 MAJOR BLOOD VESSEL VARIATION
 PERCENT PER LITTER
 DILATION OF THE ESOPHAGUS
 HEMORRHAGIC KIDNEY(S)
 DILATION OF THE BRAIN VENTRICLES
 HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY
 MISSHAPENED URETER
 HEMORRHAGIC RING AROUND THE IRIS
 PERCENT PER LITTER

284/21 345/24 336/21 329/22 355/23 320/21 266/20 353/25
 18/7 26/9 12/9 17/9 15/6 23/10 30/14 30/11
 6.0 7.0 3.5 4.8 4.1 7.3 12.3 8.5
 5/3 7/6 31/11 3/2 22/12 28/11 6/3 8/6
 1.7 1.9 8.4 1.0 6.2 8.2 1.9 2.4
 1/1 1/1 1/1 0.3 0.4 1/1 1/1
 6/5 2/2 2/1 9/7 2/2 0.3 0.4 9/6
 2.1 0.6 0.5 3.1 0.6 1.4 1.4 2.4
 2/2 2/2 2/2 2/2 5/3 7/5 3/2 3/2
 0.7 0.6 0.6 0.6 1.7 2.4 0.8 0.8

NUMBER EXAMINED SKELETALLY
 STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED
 PERCENT PER LITTER
 HYOID UNOSSIFIED
 PERCENT PER LITTER
 14TH RUDIMENTARY RIB(S)
 PERCENT PER LITTER
 STERNEBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED
 PERCENT PER LITTER
 REDUCED OSSIFICATION OF THE 13TH RIB(S)
 PERCENT PER LITTER
 STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)
 PERCENT PER LITTER
 REDUCED OSSIFICATION OF THE SKULL
 PERCENT PER LITTER
 14TH FULL RIB(S)
 PERCENT PER LITTER
 25 PRESACRAL VERTEBRAE
 PERCENT PER LITTER

VIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 72

| STUDY NO.: | 89 | 90 | 91 | 92 | 93 | 94 | 95 | 96 |
|--|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 284/21 | 345/24 | 336/21 | 329/22 | 355/23 | 320/21 | 266/20 | 353/25 |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 27 PRESACRAL VERTEBRAE | | | 1/1 | | 2/1 | 7/2 | | 2/1 |
| PERCENT PER LITTER | | | 0.3 | | 0.5 | 2.1 | | 0.6 |
| 7TH CERVICAL RIB(S) | 2/2 | 6/5 | 1/1 | 5/3 | | | 2/2 | 1/1 |
| PERCENT PER LITTER | 0.6 | 1.7 | 0.3 | 1.8 | | | 0.7 | 0.3 |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | | | | | |
| PERCENT PER LITTER | | 0.9 | 0.3 | 0.6 | | | | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | 12/4 | 2/2 | 3/3 | 4/3 | 2/2 | 2/1 | 8/6 | 3/2 |
| PERCENT PER LITTER | 4.6 | 0.6 | 1.0 | 1.3 | 0.5 | 0.8 | 3.5 | 0.8 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE ISCHIUM | | | | | | | | |
| PERCENT PER LITTER ^A | | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| ISCHIUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB(S) - THICKENED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| REDUCED OSSIFICATION OF THE RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| CENTRA UNOSSIFIED | | 1/1 | | | | | | 2/2 |
| PERCENT PER LITTER | | 0.2 | | | | | | 0.7 |
| CERVICAL CENTRUM #1 OSSIFIED | | | 41/15 | 50/16 | 41/14 | 43/16 | | |
| PERCENT PER LITTER | | | 11.2 | 16.0 | 12.1 | 13.2 | | |
| 14TH RUDDIMENTARY RIB(S) WITH 15TH RUDDIMENTARY RIB(S) | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.3 | | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 73

STUDY NO.:

97 98 99 100 101 102 103 104

NUMBER EXAMINED EXTERNALLY

FOCAL SUBCUTANEOUS HEMORRHAGE(S)
 TWINNING

328/24 339/23 319/23 320/23 287/20 347/25 385/24 339/25

NUMBER EXAMINED VISCERALLY

RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)

PERCENT PER LITTER

328/24 339/24 319/23 320/23 287/20 347/25 385/24 339/25

1/1

0.3

MAJOR BLOOD VESSEL VARIATION

PERCENT PER LITTER

1/1
 0.3

DILATION OF THE ESOPHAGUS

HEMORRHAGIC KIDNEY(S)

DILATION OF THE BRAIN VENTRICLES

HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY

MISSHAPENED URETER

HEMORRHAGIC RING AROUND THE IRIS

PERCENT PER LITTER

THYMUS HEMORRHAGIC

PERCENT PER LITTER

BRAIN HEMORRHAGE

PERCENT PER LITTER

1/1
 0.3

1/1

0.3

NUMBER EXAMINED SKELETALLY

STERNERA(E) #5 AND/OR #6 UNOSSIFIED

PERCENT PER LITTER

328/24 339/24 319/23 320/23 287/20 347/24 385/24 339/25
 34/14 23/13 32/11 27/10 12/6 14/7 12/7 37/13
 9.6 6.6 9.0 8.5 4.1 3.7 3.1 11.2

HYOID UNOSSIFIED

PERCENT PER LITTER

14TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

STERNERA(E) #1, #2, #3 AND/OR #4 UNOSSIFIED

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE 13TH RIB(S)

PERCENT PER LITTER

STERNERA(E) MALALIGNED(SLIGHT OR MODERATE)

PERCENT PER LITTER

REDUCED OSSIFICATION OF THE SKULL

PERCENT PER LITTER

13/10 19/9 8/7 3/3 15/8 2/2 14/7 5/5
 4.5 5.6 2.7 1.0 5.2 0.5 3.7 1.7
 1/1 2/2 2/2 1/1 2/2 16/9 8/3 11/7
 0.3 0.6 0.6 0.3 9/5 4.1 2.4 3.4
 4/3 2/1 8/5 9/5 2/2 1/1 1/1 1/1
 1.1 0.5 2.5 3.0 0.7 1/1 1/1 1/1
 3/3 3/2 1/1 1/1 0.3 0.3 0.3 0.3
 0.9 0.8 0.3 0.3 1/1 1/1 1/1 1/1
 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3

VII. INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 74

STUDY NO.:

| | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 |
|---|--------|--------|--------|--------|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 328/24 | 339/24 | 319/23 | 320/23 | 287/20 | 347/24 | 385/24 | 339/25 |
| 14TH FULL RIB(S) | 1/1 | | | | | 1/1 | | |
| PERCENT PER LITTER | 0.5 | | | | | 0.3 | | |
| 25 PRESACRAL VERTebrae | | | 3/1 | 1/1 | | | | |
| PERCENT PER LITTER | | | 0.9 | 0.3 | | | | |
| ENTIRE STERNUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| 27 PRESACRAL VERTebrae | 1/1 | | 1/1 | | | | | |
| PERCENT PER LITTER | 0.5 | | 0.3 | | | | | |
| 7TH CERVICAL RIB(S) | 1/1 | | 3/3 | 1/1 | 1/1 | 4/2 | 2/2 | 2/2 |
| PERCENT PER LITTER | 0.3 | | 0.9 | 0.3 | 0.4 | 1.1 | 0.5 | 0.5 |
| REDUCED OSSIFICATION OF THE VERTeBRAL ARCHES | | | | | | 2/2 | 2/2 | |
| PERCENT PER LITTER | | | | | | 0.5 | 0.6 | |
| PUBIS UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| BENT RIB(S) | 3/2 | 4/2 | | | 12/4 | | 1/1 | 2/2 |
| PERCENT PER LITTER | 1.1 | 1.2 | | | 4.4 | | 0.3 | 0.5 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | 1/1 | | | | | |
| PERCENT PER LITTER | | | 0.3 | | | | | |
| REDUCED OSSIFICATION OF THE ISCHIUM | | | | | | | | |
| PERCENT PER LITTER(A) | | | | | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| ISCHIUM UNOSSIFIED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |
| RIB(S) - THICKENED | | | | | | | | |
| PERCENT PER LITTER | | | | | | | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

PAGE 75

STUDY NO.:

97 98 99 100 101 102 103 104

NUMBER EXAMINED SKELETALLY 328/24 339/24 319/23 320/23 287/20 347/24 385/24 339/25

REDUCED OSSIFICATION OF THE RIB(S)

PERCENT PER LITTER

1/1 0.3 2/2 0.7

CENTRA UNOSSIFIED

PERCENT PER LITTER

CERVICAL CENTRUM #1 OSSIFIED

PERCENT PER LITTER

48/16 66/16 50/18 67/17
 16.1 17.8 13.3 20.3

14TH RUDIMENTARY RIB(S) WITH 15TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

UNCO-OSSIFIED VERTEBRAL CENTRA

PERCENT PER LITTER

1/1
 0.3

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

| STUDY NO.: | 105 | 106 | 107 | 108 |
|---|---------------|--------------|--------------|-------------|
| NUMBER EXAMINED EXTERNALLY | 324/22 | 318/22 | 360/25 | 340/24 |
| FOCAL SUBCUTANEOUS HEMORRHAGE(S) TWINNING | | | | |
| NUMBER EXAMINED VISCERALLY | 324/22 | 318/22 | 360/25 | 340/24 |
| RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) PERCENT PER LITTER | | | | 1/1 0.3 |
| MAJOR BLOOD VESSEL VARIATION PERCENT PER LITTER | | | | |
| DILATION OF THE ESOPHAGUS | | | | |
| HEMORRHAGIC KIDNEY(S) | | | | |
| DILATION OF THE BRAIN VENTRICLES | | | | |
| HEMORRHAGE IN THE MEMBRANE AND VITREOUS BODY | | | | |
| MISSHAPENED URETER | | | | |
| HEMORRHAGIC RING AROUND THE IRIS PERCENT PER LITTER | | | | |
| THYMUS HEMORRHAGIC PERCENT PER LITTER | | | | |
| BRAIN HEMORRHAGE PERCENT PER LITTER | | | | |
| KIDNEY- CYST(S) PERCENT PER LITTER | 1/1 0.4 | | | |
| NUMBER EXAMINED SKELETALLY | 324/22 | 318/22 | 360/25 | 340/24 |
| STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED PERCENT PER LITTER | 54/16 16.8 | 31/12 9.9 | 24/10 6.5 | 19/8 5.1 |
| HYOID UNOSSIFIED PERCENT PER LITTER | 1/1 0.3 | | | |
| 14TH RUDIMENTARY RIB(S) PERCENT PER LITTER | 9/8 2.5 | 5/3 1.6 | 5/3 1.3 | 4/4 1.2 |
| STERNEBRA(E) #1,#2,#3 AND/OR #4 UNOSSIFIED PERCENT PER LITTER | | 1/1 0.4 | 1/1 0.3 | |
| REDUCED OSSIFICATION OF THE 13TH RIB(S) PERCENT PER LITTER | 10/5 3.2 | 9/6 2.9 | 6/5 1.6 | 11/5 2.9 |
| STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) PERCENT PER LITTER | | 2/2 0.5 | | |

WIL INDIVIDUAL HISTORICAL CONTROL DATA
 CHARLES RIVER COBS CD RATS

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

| STUDY NO.: | 105 | 106 | 107 | 108 |
|---|--------|--------|--------|--------|
| NUMBER EXAMINED SKELETALLY | 324/22 | 318/22 | 360/25 | 340/24 |
| REDUCED OSSIFICATION OF THE SKULL | | | | |
| PERCENT PER LITTER | | | | |
| 14TH FULL RIB(S) | | | 1/1 | 6/1 |
| PERCENT PER LITTER | | | 0.3 | 1.6 |
| 25 PRESACRAL VERTEBRAE | | | | |
| PERCENT PER LITTER | | | | |
| ENTIRE STERNUM UNOSSIFIED | | | | |
| PERCENT PER LITTER | | | | |
| METACARPAL(S) AND/OR METATARSAL(S) UNOSSIFIED | | | | |
| PERCENT PER LITTER | | 1/1 | | |
| 27 PRESACRAL VERTEBRAE | | 0.3 | | |
| PERCENT PER LITTER | 5/4 | 3/2 | 5/5 | 7/5 |
| 7TH CERVICAL RIB(S) | 1.4 | 1.0 | 1.3 | 2.3 |
| PERCENT PER LITTER | | | | 1/1 |
| REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES | | | | 0.3 |
| PERCENT PER LITTER | | | | |
| PUBIS UNOSSIFIED | | | | |
| PERCENT PER LITTER | | | | |
| BENT RIB(S) | 5/3 | 2/2 | 5/4 | 3/2 |
| PERCENT PER LITTER | 1.5 | 0.7 | 1.5 | 0.8 |
| GENERAL REDUCED OSSIFICATION OF THE SKELETON | | | | |
| PERCENT PER LITTER | | | | |
| REDUCED OSSIFICATION OF THE ISCHIUM | | | | |
| PERCENT PER LITTER(A) | | | | |
| REDUCED OSSIFICATION OF THE PELVIC GIRDLE | | | | |
| PERCENT PER LITTER | | | | |
| INTERRUPTED OSSIFICATION OF THE 13TH RIB(S) | | | | |
| PERCENT PER LITTER | | | | |
| ISCHIUM UNOSSIFIED | | | | |
| PERCENT PER LITTER | | | | |
| RIB(S) - THICKENED | | | | |
| PERCENT PER LITTER | | | | |

INCIDENCE OF VARIATIONS (FETUSES/LITTERS)

WIL INDIVIDUAL HISTORICAL CONTROL DATA
CHARLES RIVER COBS CD RATS

105 106 107 108

STUDY NO.:

324/22 318/22 360/25 340/24

NUMBER EXAMINED SKELETALLY

REDUCED OSSIFICATION OF THE RIB(S)

PERCENT PER LITTER

CENTRA UNOSSIFIED

PERCENT PER LITTER

CERVICAL CENTRUM #1 OSSIFIED

PERCENT PER LITTER

14TH RUDIMENTARY RIB(S) WITH 15TH RUDIMENTARY RIB(S)

PERCENT PER LITTER

UNCO-OSSIFIED VERTEBRAL CENTRA

PERCENT PER LITTER

1/1 1/1
0.3 0.5

49/15 46/14 48/16 50/17
15.8 14.5 13.7 14.3

WIL-15218
Velsicol Chemical Corporation

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

APPENDIX D

Study Protocol



Study Number: WIL-15218

PROTOCOL AMENDMENT II

Sponsor: Velsicol Chemical Corporation

A. Title of Study:

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

B. Protocol Modification:

1) II. PERSONNEL INVOLVED IN THE STUDY

B. WIL Study Director

John Knapp, B.S.
Manager, Developmental, Reproductive
and Neurotoxicology

C. Reason for Protocol Modification:

1) Due to the resignation of Dr. Lamb, a new Study Director has been assigned.

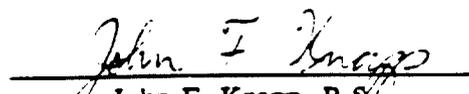
Approved By:

Prepared By:

Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-5119

WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281


John M. Bergman
Manager, Regulatory Affairs


John F. Knapp, B.S.
Study Director

9/12/94
Date

9-2-94
Date



Study Number: WIL-15218

PROTOCOL AMENDMENT I

Sponsor: Velsicol Chemical Corporation

A. Title of Study:

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

B. Protocol Modification:

1) VII. EXPERIMENTAL DESIGN

E. Method, Frequency and Analysis of Test Material Preparations

2. Frequency of Preparation

Suspensions of the test material will be prepared fresh weekly prior to dosing and stored refrigerated.

3. Analysis of Dosing Preparations for Test Material Concentration

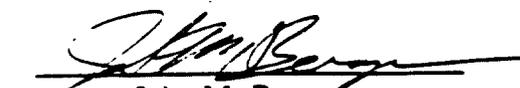
Each batch of test material prepared for administration will be prepared according to the protocol and analyzed prior to dosing.

C. Reason for Protocol Modification:

- 1) To document that dosing formulations will be prepared and analyzed prior to dosing, rather than on the day prior to dosing. This change in the protocol design was made to allow flexibility in the schedule for the preparation and analysis of dosing formulations for this study.

Approved By:

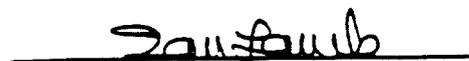
Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-5119


John M. Bergman
Manager, Regulatory Affairs

8/15/94
Date

Prepared By:

WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281


Ian C. Lamb, Ph.D.
Study Director

8-11-94
Date



PROTOCOL

A Developmental Toxicity Study of Isodecyl Benzoate in Rats

(EPA TSCA Guidelines)

Study No.: WIL-15218

For:

Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-3713

By

WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281

August 4, 1994

A DEVELOPMENTAL TOXICITY STUDY OF ISODECYL BENZOATE IN RATS

WIL Project No.: WIL-15218

I. OBJECTIVE OF STUDY

To determine the potential of the test material to induce developmental toxicity in rats.

II. PERSONNEL INVOLVED IN THE STUDY

A. Sponsor Representative

John M. Bergman
Manager
Regulatory Affairs

B. WIL Study Director

Ian C. Lamb, Ph.D.
Senior Toxicologist, Developmental, Reproductive
and Neurotoxicology

C. Study Responsibilities

1. Joseph F. Holson, Ph.D.
President, Director
2. Mark D. Nemec, B.S.
Associate Director of Developmental
and Reproductive Toxicology
3. Lisa Simon, M.B.A., B.S., M.T.(ASCP)
Supervisor of Clinical Pathology
4. Stanley E. Kopp
Systems Manager
5. Sally Keets, A.S.
Manager of In-Life Facilities
6. John Knapp, B.S.
Manager, Developmental, Reproductive
and Neurotoxicology
7. Kevin Oberholtzer, B.S.
Manager of Technical Report Writing
8. Deborah L. Little
Manager of Quality Assurance

II. PERSONNEL INVOLVED IN THE STUDY (continued)

9. Loren Severs, M.S.
Manager of Analytical Chemistry
10. Ian C. Lamb, Ph.D.
Manager of Pharmacy
11. Kerin Clevidence, B.S.
Acting Section Head I - Pathology and
Developmental Toxicology Laboratory
12. Robert Dahlgren, D.V.M., Ph.D., Diplomate A.C.V.P.
Director of Pathology

III. STUDY SCHEDULE DATA

- A. Proposed Experimental Start Date: August, 1994
- B. Proposed Experimental Termination Date: (In-Life Study) October, 1994
- C. Proposed Report Date: January, 1995

IV. TEST ARTICLE DATA

- A. Identification: Isodecyl Benzoate
- B. Lot Number: C5-8
- C. Purity: Approximately 98% mixed C₉₋₁₁ isomers, but assume 100% for dose calculations.
- D. Stability: The test material is considered stable when stored as described below.
- E. Physical Description: Clear, colorless liquid.
- F. Storage Conditions: Room Temperature.
- G. Reserve Samples: Reserve 1 gram samples of the test article will be taken in accordance with standard operating procedures and stored in the Archives at WIL Research Laboratories, Inc.
- H. Personnel Safety Data: See attached MSDS.

V. TEST SYSTEM

- A. Species: Rat
- B. Strain: Sprague-Dawley CrI:CD®BR
- C. Source: The Charles River Breeding Laboratories, Inc.
9801 Shaver Road
Portage, Michigan 49081
- D. Number on Study: 100 females (minimum of 120 purchased).
- E. Body Weight Range: Minimum of 220g at initiation of breeding
- F. Approximate Age: 80 to 120 days at initiation of breeding
- G. Identification System: Each animal will be uniquely identified by a Monel® metal ear-tag displaying the animal number. Individual cage cards will be affixed to each cage and will display the animal number, group number, study number, dosage level, sex and the date of animal arrival.
- H. Justification for Selection: This species and strain of animal have been recognized as appropriate for developmental toxicity studies. WIL Research Laboratories, Inc., has historical data on the background incidence of fetal malformations and developmental variations in this species from this same strain and source. This animal model has been proven susceptible to the effects of positive teratogenic agents.

VI. SPECIFIC MAINTENANCE SCHEDULE**A. Animal Housing**

The animals will be individually housed (except during mating) in suspended wire-mesh cages in an environmentally controlled room during the study. Nesting material will not be provided as euthanization is scheduled prior to anticipated parturition. Animals selected for study will be housed in clean cages elevated above cage-board or other suitable material that will be changed at least three times each week.

B. Environmental Conditions

Controls will be set to maintain temperature at $72^{\circ} \pm 3^{\circ}\text{F}$ and relative humidity at 40-80%. Air handling units will be set to provide approximately 10 fresh air changes per hour. Fluorescent lighting controlled by light timers will provide illumination for a 12-hour light/dark photoperiod. Temperature and relative humidity will be recorded once daily.

VI. SPECIFIC MAINTENANCE SCHEDULE

C. Drinking Water

Tap water will be available *ad libitum*. Filters servicing the automatic watering system are changed regularly according to Standard Operating Procedures. Water supplying the laboratory is analyzed for contaminants according to WIL Standard Operating Procedures.

D. Basal Diet

Purina® Certified Rodent Chow® #5002 will be offered *ad libitum* during the study. Periodic analyses of the certified feed for the presence of heavy metals and pesticides is performed and provided by the manufacturer.

VII. EXPERIMENTAL DESIGN

A. Animal Receipt and Quarantine

Each animal will be inspected by a qualified technician upon receipt. Rats judged to be in good health and suitable as test animals will be immediately placed in quarantine for a minimum of 7 to 10 days. All rats will be initially weighed and permanently identified with an ear-tag. During the quarantine period each rat will be observed twice daily for changes in general appearance and behavior. Prior to randomization, those animals judged to be suitable test subjects will be identified.

B. Randomization

At the conclusion of the quarantine period, animals judged to be suitable test subjects and meeting acceptable body weight requirements, will be cohabitated with a male. Females for which there is evidence of mating will be consecutively assigned in a block design to one control group and three test article groups of 25 rats each.

C. Breeding Procedure

A female will be cohabitated with a male rat of the same strain and source in a suspended wire-mesh cage for mating. Detection of mating will be confirmed by evidence of a copulatory plug or by a vaginal smear for sperm. Confirmation of mating will result in the female being returned to an individual suspended wire-mesh cage (assigned to a group) and the day designated as day "0" of gestation.

VII. EXPERIMENTAL DESIGN (continued)

D. Organization of Test Groups, Dosage Levels and Treatment Regimen

1. Organization of Test Groups

The dosage levels will be determined from an exploratory range-finding study (WIL Study No. 15217) and will be provided by the Sponsor Representative after consultation with the WIL Study Director. The following diagram presents the study group arrangement.

| <u>Group Number</u> | <u>Group Name</u> | <u>Test Substance</u> | <u>Dosage Level (mg/kg/day)</u> | <u>Dosage Concentration (mg/ml)</u> | <u>Dosage Volume (ml/kg)</u> | <u>Number of Females</u> |
|---------------------|-------------------|-----------------------|---------------------------------|-------------------------------------|------------------------------|--------------------------|
| 1 | Vehicle Control | Mazola® Corn Oil | 0 | 0 | 5 | 25 |
| 2 | Low Dose | Isodecyl Benzoate | 30 | 6 | 5 | 25 |
| 3 | Mid Dose | Isodecyl Benzoate | 300 | 60 | 5 | 25 |
| 4 | High Dose | Isodecyl Benzoate | 1000 | 200 | 5 | 25 |

2. Control Material

Mazola® Corn Oil

3. Route and Rationale of Test Material Administration

The route of administration will be oral since this is the anticipated route of exposure for the general population. Historically, this route has been used extensively for studies of this nature. The dosing cannulas for oral administration by gavage will be constructed of 16-gauge stainless-steel (Popper and Sons, Inc., New Hyde Park, New York).

4. Treatment Regimen

The test and control materials will be administered as a single daily dose during the period of major organogenesis, gestation days 6 through 15. All animals will be dosed at approximately the same time each day.

5. Adjustment of Dosages

Individual dosages will be calculated based on the most recent body weight to provide the proper mg/kg/day dosage.

VII. EXPERIMENTAL DESIGN (continued)

E. Method, Frequency and Analysis of Test Material Preparations

1. Method of Preparation

The specified amount of Isodecyl Benzoate will be weighed into a tared precalibrated storage container. The vehicle will be added in sufficient quantity to ensure the appropriate concentration. The suspensions will then be homogenized. After homogenization, a stir bar will be added to each formulation. While undergoing stirring the dosing suspensions will be divided into separate small containers and dispensed for daily dosing. The test suspensions will be stirred continuously during dosing.

2. Frequency of Preparation

Suspensions of the test material will be prepared fresh weekly on the day prior to dosing and stored refrigerated. If necessary, the dosing solutions will be rehomogenized each day prior to dispensing for administration to the animals. Unused portions of the dosing solutions will be discarded after administration to the animals.

3. Analysis of Dosing Preparations for Test Material Concentration

Each batch of test material prepared for administration will be prepared according to the protocol and analyzed on the day prior to dosing. Aliquots from each dose level will be obtained. The samples from each dose level will be analyzed for concentration. No other analyses of the dosing preparations will be performed during the study. Homogeneity and stability of the test material in the vehicle has been previously established by the Sponsor.

F. Maternal Observations During Gestation

1. Appearance and Behavior

Each animal will be observed twice daily for moribundity and mortality, once in the morning and once in the afternoon from gestation day 0 through 20. Clinical observations regarding general appearance or behavior will be recorded daily. During the treatment period, the animals will also be observed approximately one hour following dosing and the observations will be recorded.

2. Body Weights

Individual body weights will be recorded on gestation days 0, 6-16 and 20.

VII. EXPERIMENTAL DESIGN (continued)

3. Food Consumption

Individual food consumption will be recorded on days 0, 6, 9, 12, 16 and 20. Food intake will be reported as g/animal/day and g/kg/day for the following intervals: days 0-6, 6-9, 9-12, 12-16 and 16-20 of gestation.

4. Euthanization

Gestation day 20 by carbon dioxide inhalation.

5. Cesarean Section

The abdominal, pelvic, and thoracic cavities will be opened by a ventral midline incision and the contents examined. The uterus and ovaries will be examined. The gravid uterus will be excised, trimmed and weighed. The number of corpora lutea on each ovary will be recorded. Maternal tissues will be saved for histopathological examination in 10% neutral buffered formalin only as deemed necessary by the gross findings. The carcass of each dam will then be discarded.

6. Confirmation of Pregnancy

Uteri which appear nongravid by macroscopic examination will be opened and placed in a 10% ammonium sulfide solution as described by Salewski(1) for detection of early implantation loss.

7. Deaths and Animals Euthanized *In Extremis*

Females not surviving until the scheduled necropsy will be necropsied and the cause of death recorded, if possible. Animals not expected to survive to the next observation period (moribund) will be euthanized and subjected to a gross necropsy. Tissues may be saved for histopathological examination as needed.

The number and location of implantation sites and corpora lutea will be recorded. Recognizable fetuses will be examined externally and preserved in 10% neutral buffered formalin.

8. Abortions and Premature Deliveries

Females with evidence of abortion or premature delivery will be euthanized that day and necropsied. Recognizable fetuses will be examined externally and preserved in 10% neutral buffered formalin.

VII. EXPERIMENTAL DESIGN (continued)

G. Fetal Morphological Examination

The uterus of each dam will be opened and the number of viable and nonviable fetuses, early and late resorptions and the total number of implantation sites will be recorded. The individual uterine distribution will be documented using the following procedure. All implantation sites, including resorptions, will be numbered in consecutive fashion beginning with the left distal uterine horn, noting the position of the cervix, and continuing from the proximal to the distal right uterine horn. External, internal, and skeletal fetal findings will be recorded as developmental variations or malformations.

1. External

Each viable and nonviable fetus will be individually weighed, sexed and tagged. A detailed examination of each fetus will be conducted to include, but will not be limited to, the eyes and palate, and each finding recorded. Nonviable fetuses will be weighed, crown-rump length measured and malformations recorded. The crown-rump length of late resorptions will be recorded and the tissue discarded.

2. Visceral (Internal)

Fetuses will be examined for internal anomalies by dissection in the fresh (non-fixed) state. The thoracic and abdominal cavities will be opened and dissected using a technique described by Staples(2). This examination will include the heart and major vessels. All fetuses will be sexed internally.

The heads will be removed from approximately one-half of the fetuses in each litter and placed in Bouin's solution for subsequent processing and soft-tissue examination using the Wilson sectioning technique(3).

The heads from the remaining one-half of the fetuses in each litter will be examined by a mid-coronal slice.

All carcasses, including the carcasses without the heads, will be eviscerated and fixed in 100% ethyl alcohol for subsequent examination of skeletons.

3. Skeletal

Each eviscerated viable and nonviable fetus, following fixation in alcohol will be macerated in potassium hydroxide and stained with Alizarin Red S by a method similar to that described by Dawson(4). The skeletal examination will be made following this procedure.

VIII. DURATION OF STUDY

The quarantine, breeding and gestation phases of the study will require approximately two months. The Cesarean section aspect of the study and processing and evaluation of the fetal specimens will require approximately six weeks.

IX. STATISTICAL METHODS

All analyses will be two-tailed for a significance level of 5%. All means will be presented with standard deviations. All statistical tests will be performed by a Digital Computer with appropriate programming as referenced below.

A. Maternal In-Life Data

Mean maternal body weights and body weight gains at each interval, food consumption and organ weights will be analyzed by a one-way analysis of variance comparing each treated group, to the control group by Dunnett's test(5).

B. Cesarean Section Data

The fetal sex ratios of the control group will be compared to each treated group by the Chi-square test with Yates'(6) correction factor. The numbers of early and late resorptions, dead fetuses and postimplantation losses will be compared by the Mann-Whitney U-test(6) comparing the treated groups to the control group. The mean numbers of corpora lutea, total implantations, viable fetuses and mean fetal body weights will be analyzed by a one-way analysis of variance comparing the treated groups to the control group using Dunnett's test(6).

C. Fetal Morphological Data

The number of litters with malformations and developmental variations of the control group will be compared to each treated group by Fisher's Exact test(6).

X. QUALITY ASSURANCE

The study will be audited by the WIL Quality Assurance Unit while in progress to assure compliance with the protocol, protocol amendments, WIL Standard Operating Procedures, EPA TSCA Good Laboratory Practice Standards (40 CFR Part 792, Federal Register, August 17, 1989) and Test Guidelines for Developmental Toxicity Studies (40 CFR Part 798.4900, Federal Register, September 27, 1985). The final report will be audited by the WIL Quality Assurance Unit prior to submission to the Sponsor's Representative to assure that the final report accurately describes the conduct and the findings of the study.

This is an EPA TSCA regulated study and will be included on the WIL master schedule.

XI. RECORDS TO BE MAINTAINED

All original raw data records will be stored in the Archives at WIL Research Laboratories, Inc. Records to be retained will include, but are not limited to, the following:

- A. Protocol and protocol amendments
- B. Master protocol computer printout
- C. Teratology master schedule computer printout
- D. WIL study personnel involved in the conduct of the study
- E. Study schedule
- F. Purina® Certified feed lot records
- G. Animal receipt and identification records including purchase orders and shipping records
- H. Laboratory animal inventory
- I. Quarantine body weights and observation records
- J. Documentation of animal selection for study
- K. Test article preparation records with balance accuracy records
- L. Teratology dosing administration computer printout
- M. Breeding records including day pregnant computer archive reports
- N. Computer randomization records
- O. Gestation body weight and food consumption computer archive reports
- P. Clinical observations computer archive reports
- Q. Room temperature and humidity records
- R. Animal room cleaning records
- S. Mortality/Moribundity records
- T. Computer raw data edit records
- U. Cesarean section raw data computer records
- V. Maternal and fetal gross raw data computer records
- W. Individual fetal weights raw data computer records
- X. Fetal visceral and skeletal raw data computer records
- Y. Unscheduled deaths/euthanization records

XII. SPECIMENS AND SLIDES

Sponsor will have title to all documentation records, raw data, specimens or other work product generated during the performance of the study. All work product including raw paper data, magnetically encoded records and specimens will be retained at no charge for six months following issuance of the final report in the Archives at WIL Research Laboratories, Inc. Thereafter, WIL Research Laboratories, Inc. will charge a standard monthly storage fee for retention of such specimens. Raw data in paper or magnetic form will be retained by WIL Research Laboratories in compliance with regulatory requirements.

XIII. REPORTS

The final report will contain a summary, test article data, methods and procedures, maternal and fetal data and an interpretation and discussion of the study results. The final report will be comprehensive and shall define level(s) inducing toxic effects as well as "no-effect" level(s) under the conditions of this investigation. The report will contain all information necessary to conform with current EPA TSCA specifications.

The contents of the report will be as follows:

A. Text

1. Summary
2. Introduction
3. Objective
4. Study Design
5. Experimental Design
6. Results of Clinical Findings
7. Results of Maternal Body Weights
8. Results of Maternal Food Consumption
9. Results of Cesarean Section Data
10. Results of Fetal Morphological Data
11. Discussion and Conclusion

B. Tables

1. Summary of Clinical Observations During Gestation
2. Mean Body Weights (Grams) During Gestation
3. Mean Body Weight Changes (Grams) During Gestation
4. Summary of Food Consumption (g/animal/day) During Gestation
5. Summary of Food Consumption (g/kg/day) During Gestation
6. Summary of Maternal Survival and Pregnancy Status
7. Summary of Mean Fetal Data at Time of Laparohysterectomy
8. Summary of Fetal Malformations and Developmental Variations
9. Individual Clinical Observations Data
10. Individual Body Weights (Grams) During Gestation
11. Individual Body Weight Changes (Grams) During Gestation
12. Individual Food Consumption (g/animal/day) During Gestation
13. Individual Food Consumption (g/kg/day) During Gestation
14. Individual Dam Gross Examination at Time of Laparohysterectomy
15. Individual Fetal Data at Time of Laparohysterectomy
16. Individual Fetal Body Weights
17. Individual Gross Fetal Examination at Laparohysterectomy
18. Individual Fetal Visceral Findings
19. Individual Fetal Skeletal Findings

XIII. REPORTS (continued)

C. Appendices

1. WIL Historical Control Data (Charles River CrI:CD⁰BR Rats)
2. Analytical Chemistry Report

D. Final Report

Three copies (2 bound; 1 unbound) will be supplied.

XIV. ANIMAL WELFARE ACT COMPLIANCE

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (9 CFR). The Sponsor should make particular note of the following:

1. The Sponsor's Representative signature on this protocol documents for the Study Director the Sponsor's assurance that the study described in this protocol does not unnecessarily duplicate previous experiments.
2. Whenever possible, procedures used in this study have been designed to avoid or minimize discomfort, distress or pain to animals. All methods are described in this study protocol or in written laboratory standard operating procedures.
3. Animals that experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized as deemed appropriate by the veterinary staff and Study Director. The Sponsor's Representative will be advised by the Study Director of all circumstances which could lead to this action in as timely a manner as possible.
4. Methods of euthanasia used during this study are in conformance with the above referenced regulation.

XV. PROTOCOL MODIFICATION

Modification of the protocol may be accomplished during the course of this investigation. However, no changes will be made in the study design without the verbal or written permission of the Sponsor's Representative. In the event that the Sponsor's Representative verbally requests or approves a change in the protocol, such changes will be made by appropriate documentation in the form of a protocol amendment. All alterations of the protocol and reasons for the modification(s) will be signed by the Study Director and the Sponsor's Representative.

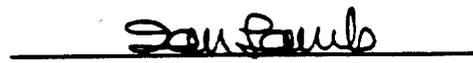
XVI. PROTOCOL APPROVAL

Velsicol Chemical Corporation
10400 W. Higgins Road, Suite 600
Rosemont, Illinois 60018-5119

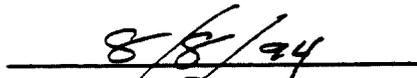
WIL Research Laboratories, Inc.
Ashland, Ohio 44805-9281



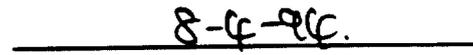
John M. Bergman
Manager
Regulatory Affairs



Ian C. Lamb, Ph.D.
Study Director



Date



Date

APPENDIX A

References

1. Salewski (Köhn), V.E. Färbemethode zum makroskopischen Nachweis Von Implantationstellen am Uterus der Ratte, Naunyn - Schm.Archiv.Fur Exper. Pathologie und Pharm., 247:367, 1964.
2. Stuckhardt, J.L. and S.M. Poppe, Fresh Visceral Examination of Rat and Rabbit Fetuses Used in Teratogenicity Testing, Teratogenesis, Carcinogenesis, and Mutagenesis, 4: 181-188, 1984.
3. Wilson, J. G., Embryological Considerations in Teratology, J. G. Wilson and Warkany, eds. Teratology - Principles and Techniques, The University of Chicago Press, Chicago, Illinois, 1965.
4. Dawson, A. B., A Note on the Staining of Cleared Specimens with Alizarin Red S, Stain Technol. 1:123-124, 1926.
5. Steel, R.G.D. and Torrie, J. H., Principles and Procedures of Statistics, McGraw Hill, New York, New York. pp. 106, 107, 114, 1960.
6. BMDP-79 Biomedical Computer Programs, University of California Press, Berkeley, California, 1979.

Date: January 23, 1991
 Supercedes: July 1, 1988

Material Safety Data Sheet



The information provided herein is applicable only to BENZOFLEX® 131 Plasticizer as manufactured by/for Velsicol Chemical Corporation.

Velsicol Chemical Corporation

Product/Material BENZOFLEX® 131 Plasticizer
Manufacturer Address Velsicol Chemical Corporation
 5600 N. River Road
 Rosemont, Illinois 60018-5184

EMERGENCY PHONE 708-698-9700

I. Product Information

Trade Name lauroyl benzoate
Synonyms C₁₁ branched alkyl benzoate
 Benzoic acid, C₁₁-branched alkyl esters
Chemical Family Benzoate ester
Chemical Formula C₁₇H₂₂O₂ (predominant component)
CAS Registry Number 131298-44-7
DOT Hazard Class Not regulated by DOT

II. Health/Safety Alert

CAUTION IRRITATING TO THE EYES. MILDLY IRRITATING TO THE SKIN.

III. First Aid Procedures

Eye Treat promptly. Flush eyes thoroughly with tap water. If irritation or other symptoms develop, immediately consult a physician.
Skin Wash skin thoroughly with soap and water. If irritation or other symptoms occur, consult a physician.
Ingestion Obtain medical attention immediately.
Inhalation Remove individual from source of exposure. Apply artificial respiration if necessary. Consult a physician.

IN ALL CASES OF EMERGENCY, CONTACT A PHYSICIAN.

IV. Note to Physician
████████████████████

Treatment is symptomatic.

V. Fire & Explosion Information
████████████████████

| | |
|---|--|
| Explosive Limits | Not known |
| Flammability | Not flammable |
| Flash Point | 174°C (345°F) OC |
| Extinguishing Media | Carbon dioxide, dry chemical foam. |
| Special Protective Equipment | In cases of a severe fire involving BENZOFLEX® 131 Plasticizer , full protective clothing and self contained breathing apparatus should be worn. |
| Special Fire Fighting Procedures | If container is intact, wet down with water to prevent overheating. Remove from fire at first opportunity. |
| Products of Combustion | May yield carbon dioxide and carbon monoxide. |
| Unusual Fire and Explosion Hazards | Water or foam may cause frothing. |
| Other | Avoid high temperatures, sparks and open flames. |
| Steps to be taken | Remove from sources of ignition. Ventilate the area. Absorb on high surface area absorbent such as sawdust, celite or diatomaceous earth. Sweep up and place in suitable container for disposal. Wash down area with water and a strong detergent. |
| Absorbents | Sawdust, dicalite, celite, diatomaceous earth. |
| Counteractants | None known |
| Incompatibles | Strong oxidizing agents |
| Reportable Quantity | None |

VI. Spill Control & Cleanup
████████████████████

Controlled incineration

VII. Product/Waste Disposal
████████████████████**VIII. Special Precautions**
████████████████████

None known

**IX. Health Hazard
Information**

Primary Route(s) of Entry Oral: No
Inhalation: Yes
Dermal/Eye: Yes

**Not Listed as a Human
Carcinogen by:** NTP, IARC, or OSHA

Acute toxicity:
Oral The acute oral toxicity (LD₅₀) in rats is greater than 5,000 mg/kg.

Dermal The acute dermal toxicity (LD₅₀) in rabbits is greater than 2,000 mg/kg.

Inhalation The acute inhalation toxicity (LC₅₀) is 3.3 mg/L (analytical).

**Other Toxicological
Information:**
Skin Irritation: Mildly irritating to the skin.

Eye Irritation: Slight to moderate conjunctival irritation which disappeared in 48 hours.

Mutagenicity: Negative in the Ames Test.

**X. Recommended General
Precautions**

Storage Store in a cool, well-ventilated area away from sources of ignition.

Ventilation Use with adequate ventilation.

**Personal Protective
Equipment** In cases where inhalation is likely, a MSHA/NIOSH-approved respirator is recommended. If eye and skin contact is likely, wear chemical goggles and impermeable gloves.

**XI. Product Information-
Hazardous Ingredients**

NFPA Rating Health: 1, Fire: 1, Reactivity: 1,
Special Properties: None

Exposure Limits OSHA PEL: None
ACGIH TLV: None

**Hazardous Ingredient(s)
(As defined by OSHA)** Isodecyl benzoate* - 98%

*Based on eye irritation

XII. Physical and Chemical Information

| | |
|--|--|
| Appearance and Odor | Colorless liquid |
| Molecular Weight | 262.38 (average) |
| Boiling Point | 161°C @ 5 mm Hg |
| Melting Point | -70°C (Glass Point) |
| Vapor Pressure (mmHg) | Not known |
| Vapor Density (Air = 1) | Not known |
| Specific Gravity (H₂O = 1) | 0.9500 |
| Solubility | Insoluble in water. Miscible in all proportions in toluene, heptane, ethyl acetate, alcohols, ketones and mineral spirits. |
| Stability | Not known |
| Reactivity | Not determined |
| Decomposition Products | There are no unusual decomposition products known for this material. |

XIII. Regulatory Information

| | |
|-------------------------|---|
| TSCA | On Public Inventory |
| RCRA | Not a listed waste |
| CWA | Not regulated |
| CERCLA | Not regulated |
| SARA 311 and 312 | Subject to reporting requirements of 40 CFR370 categories listed below: -Immediate (acute) health* |
| SARA 313 | No components listed in 40 CFR 372 |

*Based on eye irritation.

The information presented herein, while not guaranteed, was prepared by technically knowledgeable personnel and to the best of our knowledge is true and accurate. It is not intended to be all inclusive and the manner and conditions of use and handling may involve other or additional considerations.

Triage of 8(e) Submissions

Date sent to triage: 5/28/96

NON-CAP

CAP

Submission number: 13334A

TSCA Inventory: Y N **D**

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - HERD (1 copy each)

STOX CTOX EPI **RTOX** GTOX
STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

- This is the **original** 8(e) submission; refile after triage evaluation.
- This **original** submission has been **split**; rejoin after triage evaluation.
- Other:

| Photocopies Needed for Triage Evaluation | | | | |
|--|----------------------|---|---|---|
| entire document: | 0 | 1 | 2 | 3 |
| front section and CECATS: | 0 | 1 | 2 | 3 |
| Initials: <u>Jw</u> | Date: <u>4/11/96</u> | | | |

CECATS DATA: Submission # 8EHO-0295-13334 SEQ. A
TYPE (INT) SUPP FLWP
SUBMITTER NAME: Velsicol Chemical Corporation

INFORMATION REQUESTED: FLWP DATE: 03/15/95
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
0509 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/IN PROGRESS
0403 NOTIFICATION OF WORKING CONDITIONS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 02/17/95 OTS DATE: 02/21/95 SRAD DATE: 03/15/95

CHEMICAL NAME: Benzoate, Isodecyl CAS# 131298-44-7

| INFORMATION TYPE: | P F C | INFORMATION TYPE: | P F C | INFORMATION TYPE: | P F C |
|--------------------------|----------|---------------------------|----------|-------------------|----------|
| ONCO (HUMAN) | 01 02 04 | EPICLIN | 01 02 04 | IMMUNO (ANIMAL) | 01 02 04 |
| ONCO (ANIMAL) | 01 02 04 | HUMAN EXPOS (PROD CONTAM) | 01 02 04 | IMMUNO (HUMAN) | 01 02 04 |
| CELL TRANS (IN VITRO) | 01 02 04 | HUMAN EXPOS (ACCIDENTAL) | 01 02 04 | CHEM/PHYS PROP | 01 02 04 |
| MUTA (IN VITRO) | 01 02 04 | HUMAN EXPOS (MONITORING) | 01 02 04 | CLASTO (IN VITRO) | 01 02 04 |
| MUTA (IN VIVO) | 01 02 04 | ECO/AQUA TOX | 01 02 04 | CLASTO (ANIMAL) | 01 02 04 |
| REPRO/TERATO (HUMAN) | 01 02 04 | ENV. OCCUREL/FATE | 01 02 04 | CLASTO (HUMAN) | 01 02 04 |
| REPRO/TERATO (ANIMAL) | 01 02 04 | EMER INCI OF ENV CONTAM | 01 02 04 | DNA DAM/REPAIR | 01 02 04 |
| NEURO (HUMAN) | 01 02 04 | RESPONSE REQST DELAY | 01 02 04 | PROD/USE/PROC | 01 02 04 |
| NEURO (ANIMAL) | 01 02 04 | PROD/COMP/CHEM ID | 01 02 04 | MSDS | 01 02 04 |
| ACUTE TOX. (HUMAN) | 01 02 04 | REPORTING RATIONALE | 01 02 04 | OTHER | 01 02 04 |
| ACUTE TOX. (ANIMAL) | 01 02 04 | CONFIDENTIAL | 01 02 04 | | |
| ACUTE TOX. (ANIMAL) | 01 02 04 | ALLERG (HUMAN) | 01 02 04 | | |
| SUB ACUTE TOX (ANIMAL) | 01 02 04 | ALLERG (ANIMAL) | 01 02 04 | | |
| SUB CHRONIC TOX (ANIMAL) | 01 02 04 | METAB/PHARMACO (ANIMAL) | 01 02 04 | | |
| CHRONIC TOX (ANIMAL) | 01 02 04 | METAB/PHARMACO (HUMAN) | 01 02 04 | | |

USE: _____

TOXICOLOGICAL CONCERN: _____

SPECIES: RAT

ONGOING REVIEW: _____

NON-CBI INVENTORY: _____

LOW
MED
HIGH

YES (DROP/REFER)
NO (CONTINUE)
REFER

YES
NO

NOTE for maternal
x dev. tox. = 300 mg/kg/d
LOAEL = 1000 mg/kg bc bound
On transient maternal
body weight loss and
slight ↓ in mammary body
wt and ↓ ossification

IN TRAINING
SUBSIDI Non-Sap, Pmn P-90-549
Developmental Tox.
0, 30, 300, 1000 mg/kg/day by gavage
25 bred/group